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Table of Contents

THE GENETICAL STUDY OF KURU.

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IN the few years since Europeans first noticed the disease kuru among the Fore and neighbouring natives in the eastern highlands of New Guinea (Figure I) (Berndt, 1954a), it has been the subject of fairly extensive clinical and pathological investigation (Zigas and Gajdusek, 1957; Gajdusek and Zigas, 1958; Simpson, Lander and Robson, 1959; Fowler and Robertson, 1959). The cause of the disease, which involves rapidly progressive disorder of cerebellar function, has not yet been discovered. Furthermore, no genuine recovery or ameliorative treatment is known. Kuru continues to kill about one-half of the females and one-tenth of the males in many parts of the region concerned.

Following on the negative findings in studies of numerous environmental factors suspected of being possible causative agents of kuru and the subsequent suggestion that individuals may have a genetic predisposition towards the disease (Zigas and Gajdusek, 1957), H. N. Robson and F. A. Rhodes, during their field expedition in January, 1958, constructed about 200 pedigrees on the basis of genealogical information obtained from the natives. These data were subsequently analysed by one of us (J.H.B.), who, as a result, was led to advance a simple theory of inheritance of kuru to account for the family patterns which were discovered (Bennett, Rhodes and Robson, 1958, 1959). This genetical theory immediately suggested a number of further avenues of research into the disease. However, as was emphasized at the time, the data on which the analysis was based had been gathered from only a small part of the kuru region. Before the suggested theory of inheritance could be regarded as anything other than tentative, it was necessary to obtain and analyse pedigrees from other parts of the kuru area, to determine whether the same familial patterns were found in them, and to follow up the suggestions which arose from the original analysis. Accord-

ingly, in February, 1959, two of us (A.J.G. and C.O.A.) entered the field to collect further pedigrees and undertake follow-up studies. As some important verifications have already been made, it has seemed desirable to place on record some of the results of our investigations in the period February to July, 1959.

The Suggested Mode of Inheritance.

A primary step in the original genetical analysis was to recognize that the distribution of age of onset of the clinical symptoms of kuru is unimodal in males but bimodal in females (Bennett *et alii*, 1958) (Figure II). This led to the distinction of two classes of female victims — those with "early onset" of the disease, i.e.,

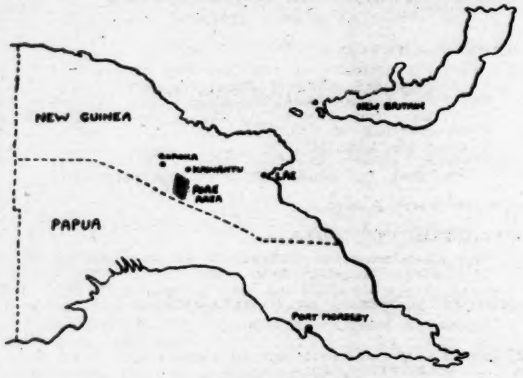

FIGURE I.
Map showing location of the kuru region in New Guinea.

before about 17 years of age, and those with later onset. It was then found that kuru was responsible for about two-thirds of the deaths amongst the mothers of "early-onset" female victims, but, on the other hand, for only about one-third of the deaths amongst the mothers of "late onset" female victims. Furthermore, with remarkably few exceptions, males who became victims of kuru had been born to mothers who also died from the disease.

After further analysis it was suggested that kuru is under the control of a single pair of autosomal alleles. These alleles we shall now call *Ku* and *ku*. The mode of inheritance is such that in females the homozygotes *KuKu* are potential "early-onset" victims, and the heterozygotes *Kuku* are "late-onset" victims. In males, on the other hand, the homozygotes *KuKu* are kuru victims and the heterozygotes *Kuku* are clinically normal. This genetical interpretation was found to be in agreement with all the collected pedigree material. Further, it provided a simple explanation not only of why the number of "early-onset" female victims was roughly the same as the number of male victims, but also of the observed phenomenon of "anticipation" or the not infrequent appearance of kuru in a victim (*KuKu*) at an earlier age than in the mother (*Kuku*). In addition, and this is of particular importance, the genetical theory allowed of the prediction that a number of individuals recorded in the pedigrees and alive and apparently in good health in January, 1958, were potential kuru victims. It thus led to the distinction of a new and important class of individuals who could be identified and subjected to close study. This might well be very useful, as for example in the search for some feature which could identify the presence of the gene *Ku* before the development of the familiar clinical symptoms. However, because of the natives' propensity towards interpretation of disease causation in terms of sorcery, the performance of complex tests on individuals, many of whom will almost certainly die from kuru, demands caution.

Area of Investigation.

The methods employed by Robson and Rhodes to obtain genealogical information from these primitive people have been described elsewhere (Bennett *et alii*, 1958). Essentially the same methods were used in the present study, although several refinements have been introduced. The original collection of pedigrees was carried out in villages situated along a road running between Okapa Patrol Post in the central part of the kuru area and Kagu to the north (Figure III). The pedigrees so obtained (comprising what has been called the R-file) contained the records of 2099 individuals, of whom 1186 were alive at the time of study. There were two principal objectives in the first few weeks of the present study. The first was to recheck the R-file material, noting any natural changes as well as other

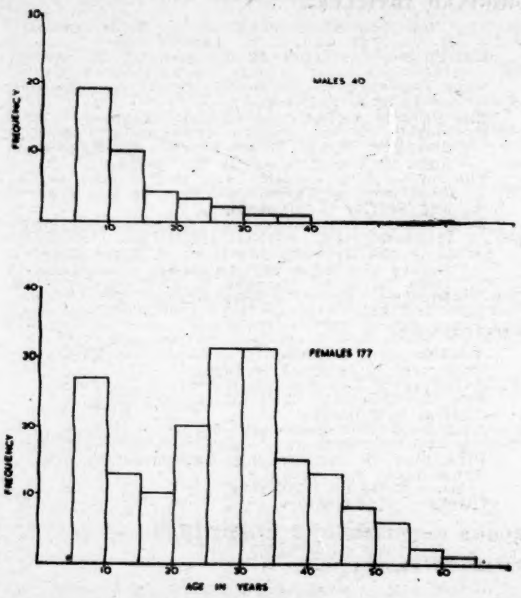

FIGURE II.
Histograms showing the distribution of age in 217 cases of kuru in the South Fore. Ninety-nine of these victims were seen by C. Gannon when on patrol in July, 1959. The others had died from kuru in the previous twelve months.

additions or corrections. The second was to construct pedigrees for members of the Keiagana, Kanite and Gimi linguistic groups in the western border region of the kuru area and also for members of the South Fore.

Results.

Almost all of the pedigrees in the R-file have now been rechecked after an interval of more than a year since they were first obtained by Robson and Rhodes. We have been very impressed by the consistency of the information supplied, especially in respect of deaths from kuru, when the same or different natives have been interrogated or reinterrogated by different observers even after such a long interval. In those relatively few cases in which a discrepancy has appeared between the classification of death in the R-file and the information obtained on rechecking this year, the latter has been reported repeatedly by all the natives questioned by us. We have therefore accepted the more recent version for inclusion in the modified-R or R′-file. Including these few corrections along with the addition of a considerable number of new family branches, 75 extra cases of kuru have been added to our records in the R′-file.

In addition to the R′-file, several new files have been set up for the other pedigrees collected from the Keiagana, Gimi and Fore linguistic groups. In all of the new pedigree material obtained in the past few months from these widely separated parts of the kuru region, we have found the same striking family patterns as in the pedigrees of the R-file (Table I).

In the pedigrees of the original collection there were 63 individuals, alive and apparently in good health in

January, 1958, who we could say were heterozygotes *Kuku* on the basis of the suggested mode of inheritance. Twenty-five of these were women, and it was predicted that they would be potential "late-onset" victims of kuru. It is therefore of some interest to note that the only deaths to have occurred among these 25 women by July, 1959, were in two individuals who had become victims of kuru.

Discussion.

The fact that the same patterns are discernible in the family data from all parts of the region examined is most encouraging. The repeated finding that about two-thirds of the mothers of "early-onset" female victims themselves *die from kuru compared with approximately one-third of* the mothers of "late-onset" victims seems to confirm our belief that there is an important difference between these two classes of females with kuru. These observations, together with the fact that mothers of male victims of kuru almost invariably die from kuru themselves, give

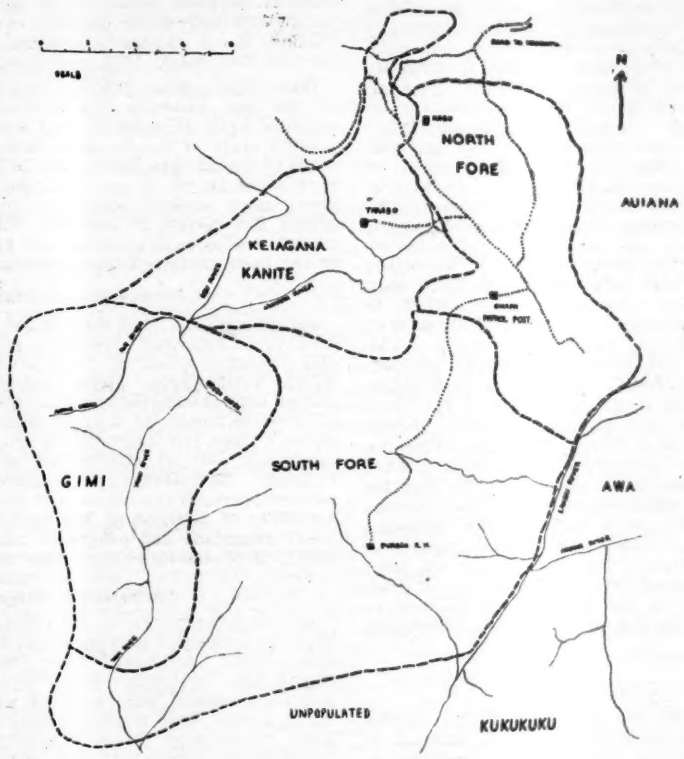

FIGURE III.
Map of the Fore and neighbouring linguistic areas. Scale in miles.

TABLE I.
Causes of Death of Mothers of Kuru Victims.

	Kuru.	Other Causes.	Total.
A. Mothers of male victims:			
Bennett *et alii* (1959)	23	5	28
Present study	55	4	59
	78	9	87
B. Mothers of "early-onset" female victims:			
Bennett *et alii* (1959)	10	6	16
Present study	70	29	99
	80	35	115
C. Mothers of "late-onset" female victims:			
Bennett *et alii* (1959)	24	51	75
Present study	52	92	144
	76	143	219

According to Berndt (1954*b*), first-cousin marriages are preferred by the Fore. However, we have found little evidence to support this. Of the few examples of first-cousin marriage which we have encountered, one of the most interesting, demonstrating segregation for kuru, is shown in Figure IV.

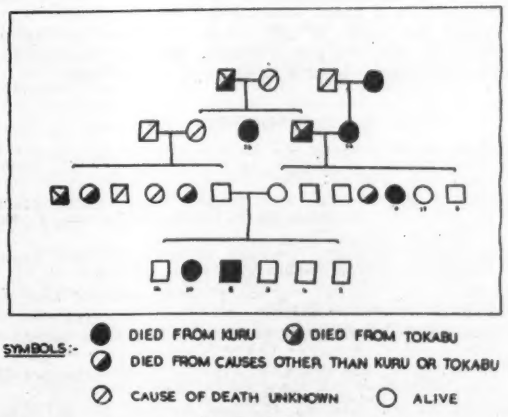

FIGURE IV.
Pedigree showing first-cousin mating with segregation for kuru.

added support to the suggested genetical basis for the disease (Bennett *et alii*, 1958).

One would imagine that the native people might have noticed that mothers of male kuru victims almost always died from the disease themselves. However, the apparent absence of any reference to this fact in their folklore would suggest that they have not observed this association. This is one of the many interesting aspects of kuru research we are at present investigating.

Kuru presents a unique problem in human population genetics. No other case is known in which a genetically determined disease of this nature is present in a population with a comparable frequency. There is virtually complete selection against homozygotes *KuKu*, since all but a few of the early-onset female victims die before the age of puberty, and male victims, although not infrequently past the age of puberty, are but rarely married. It is of some interest that the near-completeness of selection against male homozygotes *KuKu* is, in part, a consequence of the marked shortage of females in the adult population, a deficiency brought about by kuru itself. Presumably there are other powerful selective forces, which have been, and possibly still are, associated with kuru. Now that these primitive people have been brought into contact with Europeans, their society is undergoing a number of changes and some of these may be very important as far as kuru is concerned. The detailed investigation of the population genetics problem presented by kuru is therefore a matter of some urgency. During such investigations it would be as well for there to be the least possible disturbance of native society through further contact with Europeans. Otherwise the opportunity to investigate and possibly understand what has been happening among these people may be lost for all time. A registry and genealogical record of all persons in the affected area should prove invaluable for following any changes which may take place in the population structure and composition. The assembling of such records presents real practcal difficulties, but most of these have been overcome and we are now well on the way to completing these records for the 20,000 to 30,000 individuals concerned.

Acknowledgements.

The present study, which has arisen out of the investigation of kuru initiated by Professor H. N. Robson, of the Department of Medicine, University of Adelaide, in January, 1958, would not have been possible but for the generous assistance of the Papua and New Guinea Department of Public Health and the University of Adelaide. Grateful acknowledgement is due to the Rockefeller Foundation for a grant which has made it possible for us to extend the scope of this work. We are particularly indebted to Mr. Carroll Gannon, Medical Assistant at Okapa, for much valuable assistance in the field.

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NON-SPECIFIC ARTHRITIS IN CHILDREN: A REVIEW OF 105 CASES, 1931 TO 1958.[1]

By Peter Kudelka,
Melbourne.

In an attempt to gain evidence as to whether non-specific arthritis is a disease entity or merely a classification for mild or atypical forms of recognized joint diseases, a review was made of 105 consecutive cases at the Orthopædic Section, Royal Children's Hospital, Mount Eliza, Victoria, between September, 1931, and June, 1958.

Our investigations followed two lines: first, an analysis of the case histories and clinical progress of the 105 patients while in hospital, and secondly, a review of the present state of health of as many of these patients as could be traced. Six patients are at present in the hospital; to the remainder a *questionnaire* was posted, inquiring about their present condition, and requesting them to attend for review if possible. Fifty-seven (58%) satisfactory replies were received, and 21 of these patients have so far been examined and radiologically examined by us.

Selection of Cases.

All the case histories filed under "non-specific arthritis", "traumatic arthritis", "infective arthritis", "periarthritis" and "allergic arthritis" were studied, and all cases in which tuberculosis, direct bacterial infection, foreign bodies, osteochondritis and fracture had been excluded by all possible means, as detailed below, were included in the series. Thus the diagnosis of non-specific arthritis was essentially one of elimination of recognized causes of arthritis. Nevertheless, we believe that a characteristic pattern pervades the series, and if, indeed, the title covers a number of diseases, as has been suggested, they have so many diagnostic and prognostic features in common as to justify preliminary classification under one heading.

Differential Diagnosis.

It is of interest that of 108 patients admitted to hospital with the diagnosis of non-specific arthritis, 11 were found subsequently to have other conditions, as follows: tuberculous arthritis, four; pyogenic arthritis, two; Perthes's disease, two; purpura with hæmarthrosis, one; Still's disease, one; retroperitoneal neoplasm, one. Furthermore, three other cases of multiple simultaneous joint involvement associated with pyrexia and hepatosplenomegaly were excluded.

Incidence.

As all grades of severity of non-specific arthritis were met with in the series, it is possible that mild forms pass unrecognized in the community. In general, the number of admissions to this hospital under this diagnosis has been rising in recent years; there were 13 admissions for this condition during the last 12 months. Over the same period of 27 years in which the 105 patients with non-specific arthritis were admitted, 265 patients with bone and joint tuberculosis, and 188 patients with Perthes's disease were admitted.

Age and Sex Incidence.

The age and sex incidence are as follows. There were 41 males and 64 females in the series, their ages varying from two to 14 years, with perhaps slight peaks at two to four years, and nine to twelve years. The youngest patient was aged 14 months. What is perhaps a similar condition is seen in young adults, who are above the admission age for this hospital.

Joints Affected.

The weight-bearing joints were chiefly affected. In most cases the condition was monarticular. The right and left sides were equally affected. Occasionally two joints, or rarely three, were affected, sometimes concurrently and

[1] Read at a clinical meeting at the Royal Children's Hospital, Melbourne, on August 19, 1958.

sometimes consecutively. It may be argued that these few cases were manifestations of atypical rheumatic fever or juvenile rheumatoid arthritis, which latter has been recently described as having a 40% monarticular onset (Grokoest *et alii*, 1957; Rose, 1958); but the lack of the transient quality of rheumatic fever, joint abnormality, the lack of tendency to involvement of the small joints of the hands and feet with centripetal progress, and the lack of systemic symptoms (Fletcher, 1947) must be our justification for including them here. The joints involved were as follows:

One hip	41 cases
One knee	36 cases
Ankle	4 cases
Subastragaloid	1 case
Spine (lower thoracic, lumbar, lumbo-sacral and sacro-iliac sections)	13 cases
Shoulder	1 case
Elbow	1 case
Wrist	1 case
Hips and knees	2 cases
Knees	4 cases
Knees and ankles	1 case

There were no cases of involvement of the spine *plus* any other joint.

Symptomatology.

The onset was mainly insidious, but in a few cases it was more acute and related to trauma or throat infections. General reactions of malaise, fever and anorexia were rare, unless they were associated with other symptoms of respiratory infection. Pain was not a leading symptom except in spinal involvement, and often a limp or swelling first attracted the parents' attention. When pain was present it was of an aching quality, aggravated by exercise and exposure to cold, and relieved by heat and rest. Often several weeks or even months passed before medical advice was sought.

Past History of Patient.

No constant abnormalities of babyhood or development were recorded. Recurrent sore throats and colds were noted in 22 cases, and in 12 there was a history of a fall or recent injury. Recurrent toothache was recorded in seven cases, pneumonia or bronchitis in seven, asthma in three, "kidney trouble" (including acute nephritis) in five and psoriasis in one case. One patient had had poliomyelitis and one, primary pulmonary tuberculosis. Rheumatic fever, diphtheria, glandular fever were recorded in two cases each. Three patients had had hepatitis. In 58 cases no past illnesses were recorded. About 60% of the patients had been immunized.

Family History.

The number of siblings, or the place in the family, revealed no significent or constant features. No instance was recorded in which two children in the one family were affected. A family history of tuberculosis was obtained in 13 cases, of asthma in five cases, of rheumatic fever in two cases and of arthritis in three cases.

Patients came from all classes in the community, and equally from town and country areas. No significant incidence of disordered home life or anxiety state was recorded.

Illness Itself.

Loss of function, swelling, pain or discomfort in the joint were often the only symptoms. There were no constant features referable to the cardiovascular, respiratory, alimentary, uro-genital or neurological systems. The joint symptoms showed no "cyclical" changes; exacerbation seemed to follow excess use, or respiratory or dental infections. Three cases followed tonsillectomy, within a few days. The general health was often described as good, though there was some tendency to restlessness, irritability and decrease of appetite. Loss of weight was not a feature, and night sweats were not recorded. Dietary deficiencies did not seem constantly to be present in these patients.

Physical Examination.

No constant body type or colouring could be identified. Some patients were thin, some were described as "fat".

Examination of the affected joint showed changes which varied somewhat with the time since onset of symptoms. Early, the range of movement was limited by some pain and spasm. Swelling due to fluid in the joint was present, and the joint felt warm. Later there was often painless limitation of movement due to adhesions, and the swelling felt cool and was partly due to periarticular and synovial thickening, and partly apparent, owing to wasting of adjacent muscles. In no case was pus found in the joint, and the regional lymph glands were never acutely inflamed or even significantly enlarged. In the cases of arthritis of the intervertebral joints, limitation of movement due to pain and spasm, with localized tenderness over the affected vertebræ, was present. Girdle pain was recorded in one case.

General examination revealed evidence of tonsillar infection and cervical adenitis in 34 cases. Dental caries was present in 19 patients, and 12 had extractions whilst in hospital. Thus 53 patients (50%) had readily demonstrable foci of infection.

No cardiac or pulmonary lesion, no enlargement of the liver or spleen, and no neurological abnormalities were recorded.

Investigations.

A number of investigations were carried out in most cases, as described below. At present we have a routine set of laboratory tests, of which only estimation of the erythrocyte sedimentation rate and X-ray examination seem to be of use in following up the course of the disease. The erythrocyte sedimentation rate seems always to be abnormal at some stage of the illness, most commonly being raised early and returning to normal more slowly than the clinical symptoms subside. X-ray films of the joint were taken in all cases; some showed little or no abnormality. In protracted cases there was rarefaction of bone (most of these patients were immobilized) and decrease of joint space, but no gross destruction of the contour of the bone or of its articular surface. Cystic bone changes and soft-tissue calcification were not seen.

The results of the investigations carried out were as follows.

The hæmoglobin value was estimated in 61 cases; in 53 it was normal and in eight slightly below normal—never less than 65% (Haldane, 14·8 grammes per 100 ml. = 100%). The white cell count was nearly always normal, unless signs of infection elsewhere than in the joint appeared.

A Mantoux or tuberculin skin test was made with $^1/_{1000}$ old tuberculin, and if the result was negative the test was taken to $^1/_{100}$. Of 101 patients tested, 91 gave negative results and 10 positive results (one after receiving B.C.G. vaccination). Their arthritis was considered not to be tuberculous by the honorary surgeon because of their subsequent clinical course. Four patients were tested for avian tuberculosis; all gave negative results.

Synovial biopsy, carried out in nine cases, showed non-specific inflammatory changes only in all.

Inguinal gland biopsy was carried out in eight cases; in none were typical changes found.

Aspiration of joint fluid was carried out in 15 cases. In 11 the fluid was sterile on cultural examination, and in four cases no virus was indentified.

Culture of the urine produced a growth of *Staphylococcus aureus* in three cases and of *Bacterium coli* in two cases.

Culture of throat swabs produced a growth of *Staph. aureus* in seven cases and of beta-hæmolytic streptococci in three cases.

An X-ray examination of the chest in 37 cases revealed no obvious abnormality in the lungs.

In 34 cases Wassermann and Kahn tests were carried out, all with negative results. The gonococcal complement fixation test in 13 cases gave negative results. Serum agglutination tests for *Salmonella* and *Brucella* were performed in 37 cases, and in all the result was negative. The Casoni test, carried out in 11 cases, gave negative results in all.

The blood urea level was estimated in four cases, with results within normal limits in all. The serum cholesterol content, estimated in 11 cases, varied between 180 and 280 mg. per 100 ml.

The anti-streptolysin titre was estimated in 21 cases, and no constant abnormality was found. Sensitivity to horse serum was sought in nine cases, with positive results in three and negative results in six.

Serum protein electrophoresis was carried out in 17 cases, with the following results: normal pattern, eight cases; elevated total globulin content, one case; elevated alpha–2 globulin content, two cases; elevated gamma globulin content, three cases; elevated alpha–2 and gamma globulin contents, three cases.

Rose's test, performed in three cases, gave a positive result in one and a negative result in two.

In summary, there is no test diagnostic of non-specific arthritis. The significance of the protein electrophoretic pattern abnormality is not fully understood and the course of the condition may best be followed by the clinical symptoms and signs, erythrocyte sedimentation rate estimations and serial X-ray examinations.

Treatment.

No specific treatment is known. The pain, when present, rapidly subsided with rest of the part, and spasm usually responded quickly to traction or immobilization in plaster. The effusion was sometimes resorbed in a period of weeks, but often persisted for longer. The general principles of treatment were prolonged immobilization in plaster or on a double Thomas splint until the erythrocyte sedimentation rate and X-ray findings suggested quiescence, when gradual mobilization was tried. Sometimes the immobilization had to be resumed when pain or swelling reappeared. Nine patients had to be readmitted to hospital mostly within a few months of their discharge; most frequently the same joint was involved, but in four cases additional joints became affected to a lesser degree. Whilst the fallacy of *post hoc propter hoc* reasoning is recognized, it must be mentioned that some of the patients improved greatly after dental extraction or tonsillectomy.

Duration of Stay in Hospital.

Most of the patients remained in hospital for three to six months, but approximately 20% remained a year or longer.

Discharge from Hospital.

Six patients were discharged from hospital with a plaster jacket or brace, nine with calipers, and 17 with no external supports, but with "restricted" movements. Sixty-seven were recorded as having a normal range of movement in the affected joint. Two patients underwent arthrodesis of the hip.

Follow-Up Series.

Our follow-up series totals 58 cases. One patient died from cerebral tumour at the Royal Melbourne Hospital, 12 years after having been discharged from the Royal Children's Hospital. In Table I the other 57 cases are set out.

Thus, of 57 patients, 36 suffered no further symptoms and there was no tendency for the symptoms to recur after many years; 11 had mild symptoms not requiring medical attention; and 10 required further treatment. In three cases this consisted of arthrodesis of the hip, and one girl requires cortisone by mouth to control her joint symptoms. Finally, 51 patients suffer no disability now, whilst six others have slight but not incapacitating disability. Not one patient has developed classical generalized arthritis of the rheumatoid type. One patient developed asthma and one a duodenal ulcer, and four patients reported uneventful pregnancies.

Of the 21 patients so far examined by us, one only had marked disability — a man whose hip pain recurred five years after his discharge from hospital; clinical and X-ray examinations were suggestive of old Perthes's disease. The other 20 patients had good function, and 14 of these fell into the "four years or longer" group. Three patients with affected hips had slight limitation of rotation, one with half an inch of shortening and some thigh wasting on the affected side. Three patients with previously affected knees showed lessened stability to antero-posterior rocking of the flexed knee joint; in one the affected leg was half an inch longer than the other (measured by tape); two of these showed wasting of the affected thigh of up to one inch, one after 14 years. All the others were clinically normal, with full power and range of movement. Two X-ray pictures showed abnormality; one was that of the knee with "overgrowth" mentioned above, which showed coarsening of the trabecular pattern in the distal part of the femur two years after the patient's discharge from hospital, and another showed similar changes seven years after the patient's discharge.

Summary.

Non-specific arthritis thus appears as a subacute, predominantly monarticular, panarthritis chiefly affecting the weight-bearing joints, of obscure ætiology. It has no marked familial predisposition, but has, perhaps, an

TABLE I.

Results of Follow-up Investigation.

Years Since Discharge from Hospital.	Total Number of Cases.	No Symptoms.	Mild Symptoms.	Further Treatment.	Disability Now.		Joints Affected.
					Nil.	Some.	
1	4	4	—	—	4	0	Hips 3, spine 1.
2	13	8	3	2	10	3	Hips 5, spine 1, subtarsal joints 1, knees 5, ankle 1.
3	4	3	—	1	4	0	Hips 1, spine 1, knee 1.
4	7	2	4	1	7	0	Hips 7, spine 1, knee and ankle 1, knees 4.
5 to 10	15	10	1	4	12	3	
10 to 15	8	6	1	1	8	0	Hips 1, spine 2, ankle 1, knee 4.
15 to 20 Over 20	4 2	2 1	1 1	1 0	4 2	0 0	Hips 2, ankle 1, knee, ankle and hip 2, spine 1.
Totals ..	57	36	11	10	51	6	

association with infection, either respiratory or dental, and a less marked association with minor degrees of trauma. It can resolve apparently completely, or run a protracted course, withous pus formation or septicæmia, to ultimate loss of articular cartilage and fibrous ankylosis. It is favourably influenced by rest of the joint during the acute stages, and by eradication of foci of infection if these are found. Poor prognostic features seem to be multiple joint involvement and delay in the subsiding of symptoms with immobilization; but there does not appear to be an enhanced susceptibility to further arthritic or other disease processes in subsequent years. Thus in general the condition has a good prognosis.

Over the years many drugs have been tried — the salicylates, antibiotics (systemic and intraarticular administration), "Butazolidin" and recently the adrenocorticoids; not any of these are thought to be "curative" or to have a specific role in treatment. Perhaps the recent suggestion of low doses of a wide-spectrum antibiotic over a period is worthy of trial.

Theories about the ætiology of this condition have ranged from traumatic, viral, allergic, toxic and infective to many others. The findings of an association with bacterial foci elsewhere suggest a relationship; but whether this is via an antigen-antibody mechanism or some aberrant intracellular "L" form of these organisms, similar to that described by Professor Brown, of Washington, is not known. The theory of infection by virus needs confirmation by means of direct culture or perhaps serological tests. Investigations such as protein electrophoresis, Rose's test or the "Latex" test (Plotz and Singer, 1956) may aid us in the future.

Until the ætiological factors have been conclusively identified, treatment must remain symptomatic; but the association with an "infective focus" is therapeutically suggestive, and seems at the moment to give the most hopeful point of attack on this difficult condition.

Acknowledgements.

This review was made possible by the advice and assistance of the Medical Superintendent of the Royal Children's Hospital, Dr. D. Galbraith, and also of the Assistant Medical Superintendent, Dr. J. M. Davies. Mr. J. B. Colquhoun and Mr. E. E. Price gave much helpful advice and permission to review patients in their care. Miss M. E. Towler and my wife rendered invaluable assistance in the preparation of data.

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SOME OBSERVATIONS ON FŒTAL HEART IRREGULARITIES.

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IN 1893, von Winchel for the first time drew attention to fœtal heart irregularities as a sign of fœtal asphyxia in utero. It has now become established teaching that irregularities in the fœtal heart rate and meconium staining of the liquor are the most important signs of fœtal distress. However, the cause and mechanisms by which these abnormalities are produced have not yet been elucidated, and their true significance is still uncertain. Also, little has been written concerning the relationship of the occurrence of fœtal heart irregularities to the infant's condition at birth.

The main factors which have been incriminated in the production of fœtal heart irregularities are (i) conditions in which placental blood flow is diminished, (ii) pressure on the cord, (iii) direct pressure on the fœtal head. The last-mentioned theory has recently been elaborated by Prystowsky. He maintains that fœtal bradycardia is a vagal effect due to medullary ischæmia, which in turn is produced by increased intracranial pressure.

This paper deals with an unselected series of 111 consecutive deliveries. In these the following factors have been studied: (i) incidence of fœtal heart irregularities; (ii) the relationship of these irregularities to (*a*) the infant's condition at birth, (*b*) the presence of meconium staining of the liquor, (*c*) the time of occurrence during labour, (*d*) parity of the mother, (*e*) the association of abnormal presentations and positions.

Selection of Material.

The clinical material consisted of all patients admitted to the Professorial Unit at the Royal Women's Hospital, Melbourne, during the month of March, 1958. Three cases of multiple pregnancy were excluded.

The criteria of fœtal heart irregularity have been taken as a heart rate below 120 or above 160 per minute, or any irregularity of the rhythm. The criterion of a satisfactory condition of the infant at delivery was that rhythmic respiration was established spontaneously, with no other resuscitative measure than routine clearing of the airway.

The following observations were made.

Babies Needing Resuscitation.

In the 111 cases under discussion, 97 infants did not require any special resuscitative measures. Thirteen required resuscitation; of these 11 gave no further cause for concern, and two died soon after delivery. One was still-born.

In the whole series there were 18 cases in which fœtal heart irregularity occurred.

Of the 11 infants that survived and required resuscitation, only four exhibited no fœtal heart irregularities. In three of these four cases meconium-stained liquor was noted to drain from the mother during labour. Thus there was only one in the series of 111 cases in which resuscitation was required without previous observation of fœtal heart irregularity or meconium staining of the liquor. In this case the infant had the cord tightly around his neck at delivery.

These observations are summarized in Table I.

Details of Fatal Cases.

CASE I.—Neonatal death occurred in this case. No fœtal heart irregularity was noted during labour. The membranes ruptured just before delivery, and the liquor was heavily meconium-stained. The infant only gave a gasp. Autopsy revealed atelectasis.

CASE II.—This also was a case of neonatal death. The mother had had repeated ante-partum hæmorrhages between 26 and 32 weeks' gestation. Labour commenced at 32 weeks' gestation and after three hours the infant was delivered by the breech, with assistance. The infant had a strong heart beat, but rhythmic respirations were not established. The fœtal heart had been satisfactory during labour. Autopsy revealed absence of the left kidney and hypoplasia of the right kidney.

CASE III.—This was a case of still birth. The mother was admitted to the hospital at 42 weeks' gestation for medical induction of labour because of excess weight-gain. The induction was successful, and satisfactory labour followed. Twenty-four hours after the onset of labour, it was noted that the patient had a pulse rate of 120 per minute and that her temperature was 99° F. At the same time dark brown staining of the perineal pad was noted, and cervical smears were taken. Five hours later, offensive liquor was found to be draining from her. Treatment with penicillin and "Sulphatriad" was commenced. Shortly after this, the absence of the fœtal heart was noted. The patient was

delivered 24 hours later of a still-born infant. The autopsy report read as follows:

> The lungs were dense purple in colour with few subpleural petechial hæmorrhages. Trachea and bronchi were filled with thick viscid greenish meconium-like material. (This was also seen filling the stomach.)
>
> On microscopy the lungs showed marked macerative changes. There were also dense collections of leucocytes seen throughout with numerous collections of bacteria.

On the basis of the foregoing findings, the diagnosis of congenital pneumonia was made. It is interesting to note that the intrauterine infection of the fœtus occurred when the membranes were still intact.

TABLE I.

State of Fœtal Heart and Liquor.	Condition at Birth Satisfactory.	Resuscitation Necessary and Effective.	Stillbirths and Neonatal.	Total.
Fœtal heart regular:				
No meconium staining of liquor.	85	1	1	87
Liquor meconium-stained	1	3	2	5 (+1 breech)
Total	86	4	3[1]	93
Fœtal heart irregular:				
No meconium staining of liquor.	8	3	0	11
Liquor meconium-stained	2 (+1 breech)	4	0	6 (+1 breech)
Total	11	7	0	18
Fœtal heart rate more than 160:				
No meconium staining of liquor.	3	1	0	4
Liquor meconium-stained	1	0	0	1
Total	4	1	0	5
Fœtal heart rate less than 120:				
No meconium staining of liquor.	6	2	0	8
Liquor meconium-stained	1	4	0	5
Total	7	6	0	13

[1] These consisted of two neonatal deaths and one stillbirth.

The Relationship of Parity to the Incidence of Fœtal Heart Irregularity.

Of the 111 patients, 37 were primigravidæ and 74 were multigravidæ. In 10 of the 37 primigravidæ irregularities of the fœtal heart were detected; six infants required subsequent resuscitation. In eight of the 74 multigravidæ fœtal heart irregularity was detected; only one infant required resuscitation.

The Relationship of Fœtal Heart Irregularity to the Stage of Labour and its Subsequent Management.

In this series, labour was artificially induced in 18 cases — in nine by medicinal stimulation with "Infundin" and in the other nine by artificial rupture of the membranes.

Fœtal heart irregularity occurred in three out of the nine cases of medical induction and in one of the nine surgical inductions.

Of the four cases in which fœtal heart irregularity was associated with induced labour, three are summarized below.

CASE IV.—A multigravida, 43 years old, Rh-immunized, was admitted to hospital at term for induction of labour. She had previously had an Rh-immunized baby, and the result of the indirect Coombs test became positive at 40 weeks' gestation. Artificial rupture of the membranes with a Drew Smyth catheter was performed, and 18 oz. of yellowish liquor were obtained. The fœtal heart rate was satisfactory after the artificial rupture of the membranes, but about four hours later it became slow and irregular. The patient at that time complained only of backache and had no palpable contractions. No cord was felt per vaginam. She was given oxygen by intranasal administration. The fœtal heart became normal again during the next hour, although occasional slowing was observed even six hours later.

The next day she was given "Pitocin" by the intravenous drip method (5 units of "Pitocin" per litre) with no effect; the procedure was repeated 24 hours later with 10 units per litre. This time the induction of labour was successful, and the patient was normally delivered 12 hours after the commencement of the "Pitocin" drip therapy. The fœtal heart remained satisfactory till just before delivery, when sudden slowing was observed. The condition of the infant was satisfactory after resuscitation; 24 hours after delivery an exchange transfusion was given.

CASE V.—A primigravida, aged 19 years, was admitted to hospital for medical induction of labour at 43 weeks' gestation, with a high head. After the fourth dose of "Infundin" (3 min.), the fœtal heart rate became irregular. The medical stimulation was discontinued. The patient was sedated with chloral hydrate (30 grains). The fœtal heart rate rapidly returned to normal.

The patient came into spontaneous labour five days later. Fœtal heart irregularity occurred again during the second stage. The patient was delivered by forceps. The infant's condition was satisfactory.

CASE VI.—A multigravida, aged 38 years, was admitted to hospital for medical induction of labour, at 41 weeks' gestation, as she was known to have a small pelvic outlet. After the second dose of "Infundin" the uterus became tonically contracted, and the fœtal heart became slow and irregular. She was given amyl nitrite, which relaxed the uterus for a short period only, so that the patient had to be given an ether anæsthetic. This relaxed the uterus, with complete recovery of the fœtal heart.

TABLE II.

Type of Delivery.	No Fœtal Heart Irregularity.	Fœtal Heart Irregularity.	Total.
Normal	79	8	87
Forceps	9	8	17
Breech	2	1	3
Lower segment Cæsarean section	3	1	4

The patient came into spontaneous labour ten days later. The fœtal heart rate became slow again in the second stage. She was immediately delivered by forceps. The infant's condition at birth was satisfactory.

It is noteworthy that in all these cases the fœtal head was not engaged at the time of the patient's admission to hospital.

Spontaneous Labour.

Of the 17 cases in which fœtal heart irregularity occurred in established labour, it occurred during the first stage in seven and during the second stage in 10. The following are summaries of the management of the patients in whom fœtal heart irregularity occurred during the first stage.

CASE VII.—A primigravida, aged 21 years, was admitted to hospital early in the first stage of labour. She began to vomit very soon afterwards, so that intravenous dextrose therapy became necessary early in labour. Twenty hours after the onset of labour, the fœtal heart rate exceeded 160 per minute. The fœtal head was still quite high at the time. The patient was given oxygen by intranasal administration, and the fœtal heart rate returned to normal during the next two hours. She required forceps delivery five hours after the onset of fœtal heart irregularity for a delayed second stage. The infant's condition at birth was satisfactory.

CASE VIII.—A primigravida, aged 20 years, was admitted to hospital early in labour. The head was not engaged at the time. Labour progressed slowly, but she was not distressed. After 30 hours' mild labour the fœtal heart rate dropped below 120 per minute. Pelvic examination revealed that the os was dilated sufficiently to admit two fingers, and the membranes were intact. She was given chloral hydrate (30 grains). The fœtal heart rate returned to normal during the next three hours. The membranes ruptued four and a half hours after the onset of fœtal heart irregularity, thick green liquor draining away. Owing to some delay in notifying the medical officer in charge, the

TABLE III.

Clinical Data in 18 Cases in which Fœtal Heart Irregularity Occurred.[1]

Case Number.	Increased Fœtal Heart Rate. (<160 per Minute.)	Decreased Fœtal Heart Rate. (>120 per Minute.)	Time before Delivery when Fœtal Heart Irregularity Occurred.	Duration of Fœtal Heart Irregularity.	Time between Delivery and Rupture of Membranes.	Colour of Liquor.	State of Infant at Delivery.	Parity of Mother.		Fœtal Heart Irregularity Occurred during				Position of Presenting Part on Patient's Admission to Hospital.	Presentation or Fœtal Position at Delivery.	Treatment Given.	Mode of Delivery.	Remarks.
								Primigravida.	Multigravida.	Induced Labour.	Spontaneous Labour.	First Stage.	Second Stage.					
			h. m.	h. m.	h. m.													
1	+		7 30	2 0	3 15	Clear.	S.	+			+	+		N.E.	Vx. L.O.A.	Oxygen intranasally.	Fc.	Indication for Fc, delayed second stage.
2	+		14 15	4 50	1 15	Clear.	R.	+			+		+	E.	Vx. L.O.	Delivery.	Fc.	Indication for Fc, fœtal distress, delayed second stage, rotation under general anæsthesia, O.P. to O.A.
3	+		4 0	6–7 0	9 0	M.S.	R.	+			+	+		N.E.	Vx.	Oxygen intranasally, sedation, delivery.	L.U.C.S.	Contracted pelvis, failed trial of labour.
4	+		9 25	15 0	12 40	Clear.	S.		+		+	+		N.E.	Vx. L.O.A.	Nil.	N.	Bipartate placenta, velamentous insertion of the cord.
5	+		6 30	15 0	6 45	Clear.	S.		+		+	+		N.E.	Vx. L.O.A.	Nil.	N.	
6		++	16 30	5 0	0 25	M.S.	R.	+			+	+		N.E.			N.	
7		+++	6 0	1 0	0 15	M.S.	R.	++			++	++		N.E.	Face.	Sedation.	N.	
8		++	5 30		5 0	M.S.	R.	++			+	+		N.E.	Vx. L.O.A.	Sedation.	Fc.	Ante-partum hæmorrhage at 32 to 40 weeks. Indication for Fc, delayed second stage.
9		+	10 days	29 0	3 0	Clear.	S.	+		+				N.E.	Vx. L.O.A.	Sedation.	N.	Incoordinate uterine contractions occurred after medical stimulation associated with fœtal heart irregularity.
10		+					S.	+			+		+	N.E.	Vx. L.O.A.	Oxygen intranasally, M.R.	Fc.	Indication for Fc, delayed second stage.
11		+	0 55	0 55	Premature delivery M.R.	Clear.	R.	+			+		+	E.	Vx. L.O.A.	Oxygen intranasally, delivery.	Fc.	Indication for Fc, fœtal distress. Premature M.R.
12		+	(*a*) Nine days. (*b*) Before delivery.	30 0	0 65	M.S.	S.	+		+	+		+	N.E.	Vx. L.O.A.	Sedation.	Fc.	Failed medical stimulation five days before delivery. Associated with fœtal heart irregularity. Indication for Fc, delayed second stage. Fœtal distress.
13		+	(*a*) Two days. (*b*) Before delivery.	8 0	A.R.M. 2 days.	Clear.	R.		+	+	+		+	N.E.	Vx. O.A.	Oxygen intranasally.	N.	Erythroblastosis fœtalis.
14		+	(*a*) Eleven days. (*b*) Before delivery.	Till anæsthetized.	3 55	Clear	S.		+	+	+		+	N.E.	Vx. O.A.	Anæsthesia, delivery.	Fc.	Medical stimulation, tonic uterine contraction, fœtal heart irregularity, narrow outlet.
15		+	0 10	0 10	0 10	Clear.	S.		+		+		+	E.	Vx. O.A.	Delivery.	Fc.	Indication for Fc, delayed second stage. Fœtal distress.
16		+	0 15	0 15	0 40	Clear.	S.		+		+		+	N.E.	P.O.P.	Delivery.	Fc.	Indication for Fc, delayed second stage. Fœtal distress, delivered as P.O.P.
17		+	0 10	0 10	6 15	Br.	S.		+		+		+	N.E.	Br.		Br. extraction.	Membranes ruptured before onset of labour. Hydramnios, hypospadias.
18		+	0 30	0 30	2 40	M.S.	S.		+		+		+	N.E.	Vx. O.A.		N.	Green liquor drained on admission to hospital.

[1] A.R.M., artificial rupture of membranes; Br, breech; E, engaged; Fc, forceps; L.U.C.S., lower uterine Cæsarean section; M.S., meconium stained; N, normal; N.E., not engaged; O.A., occipito-anterior; P.O.P., persistent occipitio-posterior; R, resuscitated; S, satisfactory; Vx, vertex; M.R., rupture of membranes.

patient was delivered normally 50 minutes after the dirty liquor had been noted. The baby required resuscitation.

CASE IX.—A primigravida, aged 22 years, was admitted to hospital in early labour with face presentation. After 30 hours' labour the fœtal heart rate was noted to be less than 120 per minute, and irregular. The presenting part was still very high at the time. The patient was given one-sixth of a grain of heroin. The fœtal heart rate returned to normal during the next hour. She was delivered normally six hours after the fœtal heart rate irregularity had been noted. The membranes ruptured 20 minutes before delivery. The liquor was meconium-stained. The baby needed resuscitation.

CASE X.—A primigravida, aged 21 years, was admitted to hospital four hours after the onset of labour. At the time of her admission the fœtal heart rate was noted to be irregular. On pelvic examination, no placenta or cord was felt. The membranes were intact. The patient was sedated with pethidine, 100 mg. Fœtal heart irregularity with a rate of 104 to 112 per minute was observed intermittently during the next three hours. The membranes ruptured five hours after her admission. The liquor was meconium-stained. The infant was delivered normally soon after the meconium-stained liquor had been noted. The baby needed resuscitation.

CASE XI.—A primigravida, aged 31 years, was admitted to hospital at term in mild labour. The head was very high. She was known to have a pelvis under average in size. After 20 hours' labour she had some albuminuria and acetonuria. The intravenous administration of dextrose was commenced. The fœtal heart rate was satisfactory. A vaginal examination was performed for the assessment of progress during which the membranes were accidentally ruptured. The liquor was clear. Two hours later the fœtal heart rate exceeded 160 per minute, but remained regular. She was given heroin (one-sixth of a grain) as a sedative. The fœtal heart rate did not settle in spite of sedation. The progress was unsatisfactory. Lower uterine segment Cæsarean section was performed six hours after the fœtal heart irregularity had been noted. The infant needed resuscitation.

CASE XII.—A multigravida, aged 29 years, was admitted to hospital in the first stage of labour; clear liquor was draining. A fœtal heart rate exceeding 160 per minute was noted soon after her admission. She was given chloral hydrate (30 grains) as a sedative. She had a normal delivery 12 hours later. The infant's condition was satisfactory at birth.

CASE XIII.—A multigravida, aged 33 years, was admitted to hospital five hours after the onset of labour; clear liquor was draining. Two hours after her admission to hospital the fœtal heart rate became irregular and exceeded 160 per minute. She was given chloral hydrate as a sedative. The infant's condition was satisfactory at birth.

All these patients had an unengaged head on their admission to hospital; four infants out of seven needed resuscitation when fœtal heart irregularity occurred during the first stage of labour. All infants needing resuscitation in this group were normal term babies.

Fœtal Heart Irregularity Occurring in the Second Stage of Labour.

This occurred in this group in nine instances. Eight of these nine patients were delivered normally or by forceps in less than one hour after the fœtal heart irregularity had been noted. In the remaining case, on pelvic examination œdema of the anterior lip of the cervix was found. Clear liquor was obtained on artificial rupture of the membranes. As the fœtal heart rate returned to normal after the intranasal administration of oxygen, the labour was allowed to progress. The infant was subsequently delivered two hours later by low forceps extraction for a delayed second stage.

In three of the nine cases in which fœtal heart irregularity occurred during the second stage, the infants needed resuscitation. These included one premature baby, one erythroblastotic baby (who later required exchange transfusion) and one infant delivered after difficult manual rotation under general anæsthesia.

Relationship of the Occurrence of Fœtal Heart Irregularity to Abnormal Presentations and Positions.

In the series under discussion there were: (i) 101 normal deliveries, and (ii) 10 deliveries with abnormal presentations and positions, as follows; (*a*) three breech presentations (one fœtus had heart irregularity), (*b*) two face presentations (one fœtus had heart irregularity), (*c*) five persistent occipito-posterior positions (two fœtuses had heart irregularity). Thus the incidence of fœtal heart irregularity in the second group was higher than in normal vertex presentations with anterior position.

Method of Delivery.

The method of delivery in the whole series is summarized in Table II.

Thus the few cases of fœtal heart irregularity accounted for nearly half the cases of forceps deliveries in the whole series studied. However, fœtal distress *per se* was the sole indication for only three of these forceps deliveries. In the remaining five, forceps delivery was performed for additional obstetrical indications.

The Table III summarizes the clinical data in the cases in which fœtal heart irregularity occurred.

Summary and Conclusions.

An attempt has been made to assess the incidence of fœtal heart irregularities in an unselected group of 111 consecutive births. The following conclusions can be drawn:

1. With one exception, all cases in which the infant required resuscitative measures to establish rhythmic respiration were associated with fœtal heart irregularity or meconium staining in the liquor. However, the presence of one of these signs of fœtal distress does not necessarily imply that the fœtus will subsequently require resuscitative measures after delivery.

2. When both fœtal heart irregularity and meconium staining of the liquor were present, a higher rate of resuscitative measures was needed.

3. There was a relatively high incidence of infants needing resuscitation when fœtal heart irregularity occurred in the first stage of labour, even though the fœtal heart rate had returned to normal.

4. Fœtal heart irregularity appeared to be more common in primigravidæ. Slowing of the fœtal heart rate during the first stage of labour was almost entirely limited to this group.

5. Fœtal heart irregularity following induction of labour and occurring during the first stage of labour, in primigravidæ at least, was associated with an unengaged head at the onset of labour.

6. There was a high incidence of fœtal heart irregularity in association with abnormal presentations and positions — namely, breech and face presentation and persistent occipito-posterior position.

Acknowledgement.

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THE PHRENIC AMPULLA.

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THE phrenic ampulla is a dilatation of the lower end of the œsophagus just above the level of the diaphragm, which is best demonstrated when the filled œsophagus is viewed in the inspiratory phase of respiration. The term was first used by Hasse and Strecker in 1905, although the ampulla was described by Mehnert in 1898, and Hasse and Strecker acknowledged this in their paper. The observations which follow are the results of the study of a very large number of patients; but a series of 100 cases was reviewed especially for the purposes of this paper.

Anatomical Considerations.

Laimer (1883) studied 60 cadavers in which the stomach had been filled with air and with water. He did not specifically describe the ampulla, but his work is of great value from the point of view of understanding the formation of this structure. He was the first anatomist to describe the phreno-œsophageal membrane, which he referred to as the supporting structure of the œsophagus. This membrane, which contains a considerable amount of elastic tissue, is derived from the pillars and fasciæ of the diaphragm, and splits into two layers. The descending layer is inserted into the stomach. The ascending layer is inserted into an area of constant narrowing in the lower part of the œsophagus, which was also described by Laimer, and which shows some thickening of the inner muscle fibres of the œsophagus. This author used the term "inner" rather than "circular", as he showed that most of the fibres in this layer ran obliquely and somewhat irregularly. He stated that this constriction was usually found just above the level of the œsophageal hiatus of the diaphragm, and in most cases 2 cm. above it.

Mehnert (1898) reviewed the work of Laimer, and drew attention to dilatations above and below the area of constriction which had been described by Laimer.

Hasse and Strecker (1905) described anatomical studies of the stomach as seen in the fœtus, the child and the adult, together with the changes noted when the viscus was filled and empty. The presence of an œsophageal dilatation above the diaphragm was now well known, and it had been described by a number of authors who used different names to describe it. Schreiber (1901) referred to the "epicardia", and the earlier authors Arnold (1838) and Luschka (1857) had used the terms "cardiac antrum" and "*Vormagen*"; but their descriptions did not make it clear whether these structures were above or below the diaphragm. However, Hasse and Strecker used Latin nomenclature and referred to the "ampulla phrenica", which they further show clearly in a number of illustrations.

Kahn (1906), in experiments on dogs, introduced an oval piece of wood attached by a string to a recording device into the lower part of the œsophagus, and was able to demonstrate that this region was capable of quite strong contraction.

Cunningham (1937) merely stated that the phrenic ampulla was a "fusiform expansion of the tube, of variable length and girth".

Lerche (1950) reviewed the work of Laimer in considerable detail, and made a study of the œsophagus based on dissections of 100 cadavers. Lerche describes a complex mechanism at the gastro-œsophageal junction, which he refers to as the gastro-œsophageal segment of expulsion, and which comprises (i) the constrictor cardiæ, (ii) the gastro-œsophageal vestibule, (iii) the inferior œsophageal sphincter, (iv) the phrenic ampulla and (v) the phreno-œsophageal elastic membrane.

Figure I shows diagrammatically the relationship of these areas to each other and to the diaphragm. It will be seen that considerable movement of the œsophagus is allowed through the hiatus, as it is attached only by the sling-like and elastic phreno-œsophageal membrane; this is itself attached at the level of the inferior œsophageal sphincter, which is seen to be the lower boundary of the phrenic ampulla.

The Radiographic Examination.

The radiographic examination can be conducted with the patient in the supine, the prone or the erect position, since, although the ampulla is more easily demonstrated with the patient supine or prone, it can also be shown with the patient erect, as Epstein (1957) has pointed out.

When the supine technique is used, the patient is turned so that his right side is raised slightly off the table, and he is given a large mouthful of thick barium mixture and asked to swallow it. The bolus is then watched passing

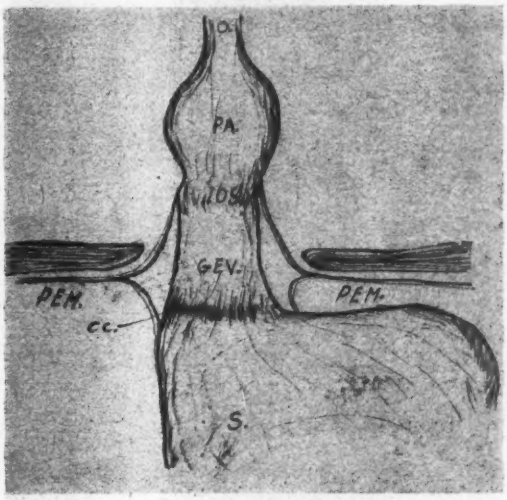

FIGURE I.

The gastro-œsophageal segment of expulsion. O., œsophagus. P.A., phrenic ampulla. I.O.S., inferior œsophageal sphincter. G.E.V., gastro-œsophagael vestibule. P.E.M., phreno-œsophageal membrane. C.C., constrictor cardiæ. S., stomach.

down the œsophagus until it commences to enter the stomach, and should minor degrees of spasm hold up the progress of the barium, it can be assisted in its passage by tilting the table toward the vertical or by giving more of the mixture. As the barium commences to enter the stomach, the patient is asked to take a deep breath and hold it. As inspiration takes place, the barium ceases to enter the stomach, the lower part of the œsophagus contracts, the portion 2 to 5 cm. above the area of contraction dilates, and a further constriction then appears at the upper limit of the dilatation. The degree of dilatation may often be increased by asking the patient to execute a Valsava manœuvre. The dilated segment of œsophagus between the two areas of contraction is the phrenic ampulla.

Should the patient continue to hold his breath, portion of the bolus will be forced back past the upper area of constriction and up the œsophagus; after this, the constriction will disappear, and the ampulla will become smaller as more barium passes in a retrograde direction. When the patient breathes out and then commences normal respiration, the dilated ampulla will usually return to a normal size, and later, when a further peristaltic wave passes down the œsophagus, the barium will again enter the stomach. Should the patient take another large breath and hold it, the ampulla will again dilate and the cycle will recommence. However, at any time that barium remains in the œsophagus, even though the amount may

be small and merely sufficient to outline the walls, ampullary dilatation can still be demonstrated on inspiration, and the more readily if the patient is prone or supine. The shape of the ampulla may vary from patient to patient, as does the position of the constriction above it, and it is also noted that there may be variations in the shape of the ampulla in the same patient, although the position of its lower border remains constant.

In some cases a concentric ring may form in the centre of the ampulla and remain constant in this position for as long as the ampullary dilatation is present. These rings have been noted by a number of observers, Inglefinger and Kramer (1953) considering them to be an active motor phenomenon. Schatzki and Gary (1953 and 1956) also describe a number of cases, most of them in elderly people, and, like those of Inglefinger and Kramer, a number of

Figure II.

these patients gave a long history of dysphagia; they do not suggest any definite ætiology, but state that the degree of dysphagia is inversely proportional to the maximum diameter of the ring. Only one case of ring formation was noted in the present series and it was not associated with dysphagia.

In Figure II both the œsophagus and the stomach contain barium, and the segment of œsophagus between the inferior œsophageal sphincter and the cardia is narrowed; the diameter of the œsophagus 2 cm. above the diaphragm is 7 mm., and 2 cm. higher it is 1 cm. (All measurements are as seen on the film, which means that there is a magnification factor of between 1% and 4%.) The patient was then asked to hold his breath, and an egg-shaped ampulla was formed (Figure III) with a diameter of 2·8 cm., whilst above the ampulla the œsophagus had collapsed and the upper limit of the expansion was sharply demarcated. A few seconds later, with the patient still holding his breath, barium was commencing to flow back up the œsophagus (Figure IV), and the upper demarcation of the ampulla had become less sharply defined. Considerable variations in shape may be noted in different patients, and two further types of ampulla are seen in Figures V and VI. Another ampulla is seen in Figure VII, and formations of this nature may at times be mistaken for herniæ unless the mechanism of ampulla formation is understood.

The above-mentioned procedures are very satisfactory from the point of view of demonstrating the ampulla in a dilated state; but it should be fully realized that the ampulla is an anatomical structure, and not dependent on inspiration or the presence of barium for its existence, as has been shown by the anatomical work discussed above.

When the œsophagus is examined radiographically with the patient in the horizontal position (prone and supine positions each have advantages) and with normal respiration, the ampulla is still clearly visible. The horizontal position is desirable as studies of the œsophagus in the erect position are both sketchy and misleading, owing to the rapidity with which the heavy barium passes down the œsophagus giving no true indication of the

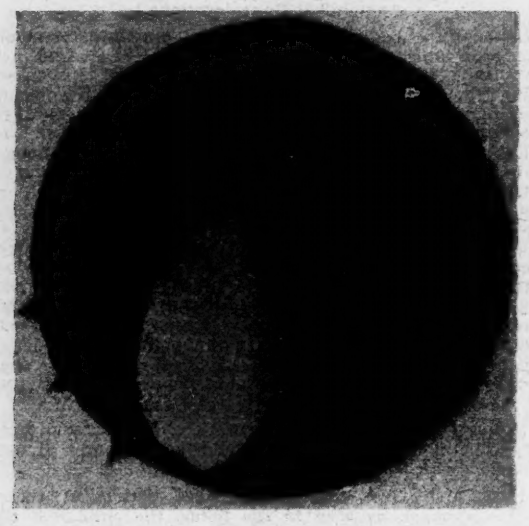

Figure III.

normal and revealing only the most advanced of pathological states. In fact, I believe that it is largely this neglect of the horizontal œsophageal examination which is responsible for the lack of appreciation of the significance of the ampulla and of difficulties in the diagnosis of hiatus hernia—not because the horizontal position is not used in the search for hernia, but because of its neglect in routine cases, which leads to lack of knowledge of the normal. As examined in the horizontal position with either thick or thin barium or with barium mixed with food, the lower part of the œsophagus still shows ampullary dilatation on normal respiration, there usually being an increase in the size of the ampulla before the bolus commences to enter the stomach.

Correlation of Anatomic and Radiographic Appearances.

The difficulty of relating fixed anatomical structures to functioning mechanisms is one which is not peculiar to this region. Palmer (1953) has shown that the œsophagogastric junction is very difficult to identify and the hiatus even more so. Pecora (1958) shows a skiagram from a case in which metal clips were attached to the hiatus at operation; these are shown well above the general level of the diaphragm. He also shows further skiagrams taken after the swallowing of balloon tubes, in which the hiatus is seen to be below the level of the diaphragm in pneumoperitoneum. Templeton (1944), in his excellent monograph, expressed doubts as to whether the ampulla seen by radiologists was identical with the anatomical structure so named, and also suggested that the ampulla might be situated below the insertion of the ascending portion of the phreno-œsophageal membrane. All this gives a very

clear indication of the difficulty experienced in fixing the anatomical points in this region, and this is, of course, due to the elastic nature of the structures involved and to the formation and nature of the phreno-œsophageal membrane.

Lerche has described the presence of two dilatations above the stomach, one of which is the gastro-œsophageal

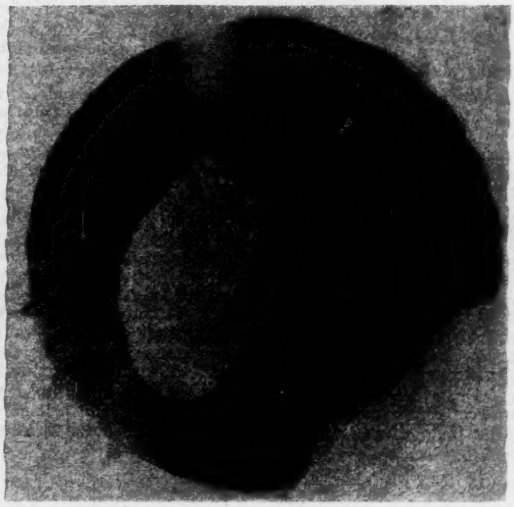

FIGURE IV.

vestibule and the other the phrenic ampulla, whereas only one dilatation is usually visible on radiographic examination of the normal œsophagus. Both Templeton (1958) and

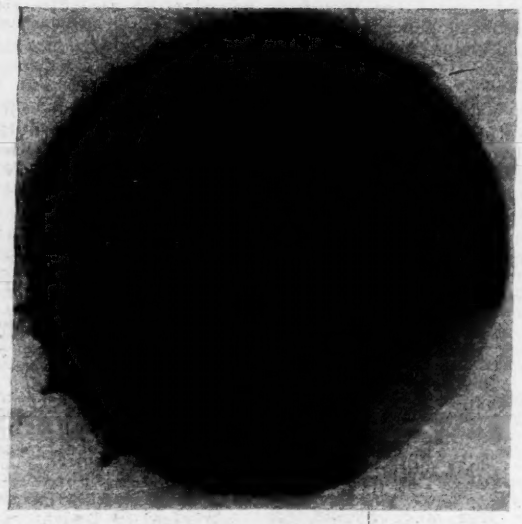

FIGURE V.

Palmer (1952) believe that the expansion which is seen radiographically is probably the gastro-œsophageal vestibule, and that as far as radiology is concerned, the phrenic ampulla does not exist.

My own view of this problem is that the key to the understanding of the anatomy is the position of the inferior œsophageal sphincter. Many anatomists and physiologists have stated that no sphincter exists in the lower part of the œsophagus; but even though there may be uncertainty on other points, there can be no doubt in the mind of anyone who has studied a number of cases by fluoroscopy that a sphincter does exist, and that it corresponds very well in position and function with the sphincter described by Laimer and by Lerche. The sphincter is usually found some 4 or 5 cm. above the cardia and 2 cm. above the diaphragm. Despite the views expressed to the contrary, it would therefore appear that one should regard the constriction which is seen above the diaphragm when the ampulla forms as the inferior

FIGURE VI.

œsophageal sphincter, as it is constant in position in the one patient, whereas the upper limit of the ampulla is inconstant and merges into the œsophagus.

Further information is provided by the pressure studies which have been undertaken in the œsophagus, although the results have not always been easy to interpret. The work of Sanchez *et alii* (1953) and of Fyke *et alii* (1956) appears to confirm the views expressed above with regard to the presence of a phrenic ampulla which is separated by a sphincter from the vestibule. The vestibule itself is usually seen in radiographs as a projection of the stomach into or through the diaphragm when the stomach is full, whereas the ampulla is usually seen after barium has filled the œsophagus so that the two structures need not be confused.

The mechanism by which the ampulla is caused to dilate on inspiration has usually been described as a "pinchcock action of the diaphragm", this phrase being used by a number of authors, notably Jackson (1922). The narrowing at the lower limit of the ampulla is well above the diaphragm. This is consistent with the fact that the inferior œsophageal sphincter contracts to produce the ampullary expansion; this is then increased on inspiration by descent of the diaphragm with resultant pulling down of the elastic phreno-œsophageal membrane which is

inserted into the inferior œsophageal sphincter; thus further narrowing below the ampulla is produced. No doubt direct pressure from a contracted diaphragm also plays a part in the formation of the ampulla; but the position of the lower margin is more in keeping with production by the sphincter and elastic mambrane than by the direct diaphragmatic mechanism.

Two cases in which large hiatus herniæ were present were studied in the present series, and in both of these the cardia was well above the diaphragm. In both cases a constriction was visible above the cardia and in the

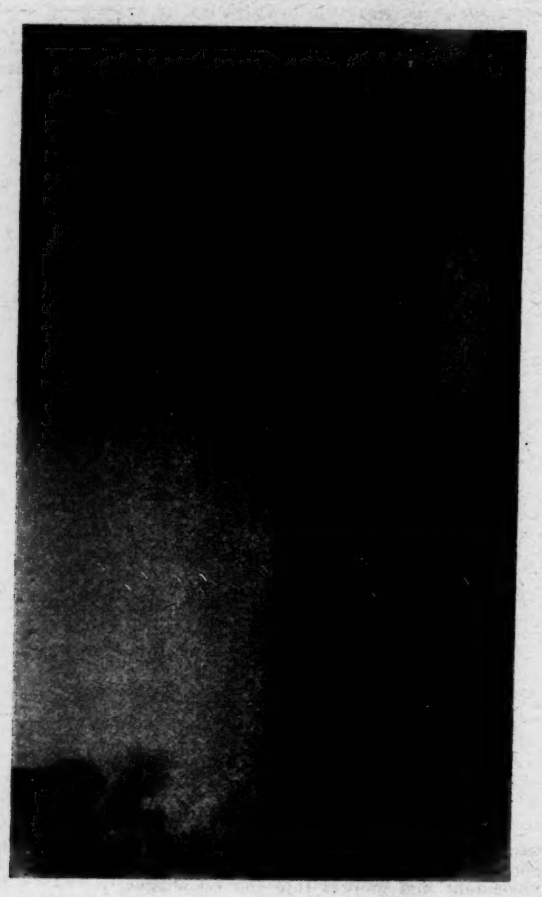

FIGURE VII.

position of the inferior œsophageal sphincter, whilst above the sphincter there was a slight dilatation due to the ampulla. Inspiration did not produce any alteration in the ampulla. This showed that in these cases the phreno-œsophageal membrane was degenerate and ineffective, so that neither the membranous nor the direct diaphragmatic mechanism was effective. There is therefore reason to believe that the expansion of the œsophagus seen above the diaphragm in radiographs is identical with that described by the anatomists as the phrenic ampulla, and furthermore, that its lower limit is the inferior œsophageal sphincter, into which is inserted the phreno-œsophageal membrane that pulls down the sphincter on inspiration.

Discussion.

It has been shown that on inspiration the lower part of the œsophagus can dilate owing to the production of an enlarged ampulla, and that this is clearly demonstrated when the œsophagus contains barium. During the course of barium meal X-ray examination, it is usual to take a number of skiagrams of the stomach. These are almost invariably taken in the inspiratory phase, so that ampullary dilatations may be produced and recorded. Should the true nature of the ampullæ so demonstrated not be appreciated, it is easy to regard these structures as hiatus herniæ, and from time to time radiographs have been published purporting to demonstrate herniæ which, in fact, have every appearance of being ampullæ. Boyd *et alii* (1956), in the course of a review of the diagnostic problem presented by hiatus hernia, state that they found the phrenic ampulla the most confusing of the conditions which simulated hernia.

However, no great difficulty should be experienced in differentiating the two conditions, so long as the relation of the ampulla to the inferior œsophageal sphincter is kept in mind, together with the behaviour of the ampulla on respiration, in which it undergoes such a characteristic cycle in the inspiratory phase.

An œsophagus which has rigid walls is unlikely to show any ampullary dilatation on inspiration, and therefore the absence of the ampullary cycle may be of assistance in the diagnosis of conditions in which the lower œsophageal wall is made rigid by carcinoma, chronic œsophagitis and other diseases. A knowledge of the ampullary cycle is also of value in the investigation of the lower part of the œsophagus for varices, in that barium can be kept moving up and down the œsophagus and any suspect segments thoroughly examined by fluoroscopy and spot radiography. Thus the difficulty arising from the usual quick passage of the bolus through this area can be overcome.

Summary.

Attention is drawn to the phrenic ampulla, which consists of a dilatation of the lower part of the œsophagus best seen on radiographic examination with the patient horizontal and holding his breath. An attempt is made to correlate the appearances described by the anatomists with the radiographic findings, and the difficulty of identifying fixed anatomical points in this region is noted. It is pointed out that it is important to recognize the phrenic ampulla in order that it should not be confused with hiatus hernia.

Acknowledgements.

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EVALUATION OF THE HEALTH OF INFANTS FED FULL STRENGTH COW'S MILK.

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AND
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THE method of infant feeding practised at the Royal Newcastle Hospital Well-Baby Clinic has been previously reported (MacMahon, Woodhill and Gibson, 1959). As a result of the findings of this previous report, a follow-up on a further series of cases was deemed necessary.

All infants discharged from the obstetric department on full strength cow's milk or on a complement of full strength cow's milk, or who were found to have been put on full strength cow's milk within the first five weeks of life were followed up. Of those discharged on complementary feedings, only those who had been put on full strength milk completely within the first five weeks of life were included.

It was planned to evaluate the results of the feeding method and the general health of the infants at four to five months of age. All the interviews and examinations were carried out by one observer (R. MacM.).

From November, 1957, to April, 1958, inclusive, 73 infants qualified according to the above-mentioned criteria; it was possible to contact only 62 of these. The reasons why the other 11 could not be evaluated are as follows: letters to five of the mothers were returned from the dead letter office, four had New Australian mothers, the mother of one baby was in Broughton Hall Psychiatric Clinic and in one case the mother was unwilling to attend. There were no deaths in the group.

Of the 62 infants seen at the survey, 13 had been changed from whole cow's milk, 21 came into the "perfect baby" category, and 28 had had various gastro-intestinal upsets or other illnesses.

Of the 13 babies in whom the feeding had been changed, it was found that most of the changes had been advised by baby health centres, local chemist or general practitioner because of relatively minor upsets (10 cases). One vomiting bout, a few hard stools or a restless period during the day were used as reasons for this change of feeding. In fact, change of feeding often appeared to be the first line of attack, even the only one, on problems of infant management. In one case the feeding was changed because of the personal preference of the mother.

Two cases of pyloric stenosis are included in this group. Both infants were put on bottle feeding with full strength cow's milk early, but were not seen again until they were referred to the hospital for investigation of vomiting and failure to thrive. In the intervening period, both had had several changes of feeding advised by other persons, because of the vomiting, without effect. After operation, both were discharged from hospital on full strength cow's milk, and have progressed well.

Of the 28 infants who exhibited any type of illness, six had had various diseases unrelated to the gastro-intestinal tract, such as measles and otitis media. The other upsets were of all grades of severity, but in no case were they of such a nature as to justify change of feeding: constipation, 11 cases; "the gastric", 7 cases; wind, 3 cases; excoriated buttocks, one case.

Most mothers in the Newcastle district refer to bouts of diarrhœa with or without vomiting as "the gastric", and in this group these bouts were all of a short-lived and not severe nature. Constipation was the commonest upset. In some cases it was only of a minor nature, but in others it was persistent. Constipation has here been taken to refer to hard, pellet-like stools. In almost all cases this ceased when the infant went on to solids.

The incidence of constipation was sufficient to require critical evaluation. It is thought that it may have been related to the fact that this survey was done in the summer months of a particularly hot summer, and that many mothers in this community are in the habit of putting excessive clothing on their infants in hot weather. Both these conditions would favour the loss of a considerable amount of fluid from the body, particularly by sweating, and the fluid requirements of such infants would be high. Darrow *et alii* (1949), discussing the disturbances of water and electrolytes in infantile diarrhœa, emphasized the importance of sweating in these conditions, and stated:

> As indicated by studies of heat balance most of the patients would have had fever if heat production had remained normal and no sweating had developed. This conclusion is in keeping with the physiologic function of sweating which is necessary for heat loss as the environmental temperature rises above 80° F. When the environmental temperature is above 92° F. all the heat loss is accounted for by evaporation.

They further stated that in such high temperatures, "in the development of dehydration, losses of water in sweat are quantitatively as important as losses in stools".

It seems likely that this high incidence of constipation is related to this and that all the fluid available has been extracted from the stools, leading to constipation. In our previous experience we had not seen any definite evidence that copious fluid should be offered to infants, and no insistence had been placed on this in the clinic. However, this survey provided us with such evidence.

In this regard Darrow *et alii* (1954), discussing water and electrolyte metabolism in infants during heat stress, when rather extreme extrarenal expenditures of water were involved, stated:

> It is doubtful if clinical observations of normal infants could demonstrate any superiority of milk with added carbohydrates over unmodified milk, provided the unmodified milk is diluted to a concentration of 50 cals per 100 mls. in hot weather or provided that the infants take sufficient additional water during hot weather.

As a result of ths study, further investigation is needed on the relationship of constipation to water loss in both breast and bottle fed infants in periods of hot weather, and into local clothing customs in our hot climate.

Summary.

Sixty-two infants born November, 1957, to April, 1958, inclusive, and fed full-strength cow's milk from within the first five weeks of life were followed up at approximately five months of age, and their health was evaluated by one observer.

The sample consisted of 85% of all possible cases. The reasons why the remaining 15% could not be followed up are cited.

An incidence of feeding changes advised by other persons (general practitioners, baby health centre sisters and chemists) is reported.

The result of the 62 medical assessments gave no reason to change the feeding of full-strength cow's milk to infants up to five months of age provided extra water is offered in hot weather.

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THE INFLUENCE OF ASCORBIC ACID AND OF MILK ON THE ABSORPTION OF THERAPEUTIC IRON.

By ILSE BRADING AND SHIRLEY A. CANTRILL,
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A PROBLEM which arises in oral iron therapy is whether additives increase assimilation of the iron. Commercially available compounds frequently contain trace elements, small amounts of vitamins or amino acids. There is, however, no evidence that these are necessary for therapy of iron deficiency anæmia, and they are usually present in amounts which are insufficient for therapy of specific deficiency states. With the exception of ascorbic acid, none of the additives appears to increase absorption of iron. The role of ascorbic acid is therefore of some interest. Moore, Arrowsmith, Welch and Minnich (1939) suggested that ascorbic acid assists in iron absorption by reducing ferric iron to the ferrous state, and by preventing oxidation of iron already in the ferrous state. They found little change in the serum iron values after oral ingestion of ferric salts, but an increase equal to or greater than that produced by ferrous salts when ascorbic acid was given with ferric salts. The vitamin also increased the changes in serum iron produced by ferrous salts.

More recently, Moore and Dubach (1955) showed that the addition of ascorbic acid to some iron-containing foods regularly increased the absorption of iron, but the effect was not observed when the ascorbic acid was injected intravenously. In these experiments the tested foods contained Fe^{59}, and it was possible to measure absorption by determining the presence and amount of Fe^{59} in the blood of volunteers who ingested the food.

This paper reports the results of experiments in rats, which were designed to confirm the value of adding ascorbic acid to therapeutic inorganic iron preparations. Ferrous sulphate solution containing a small amount of $Fe^{59}Cl_3$ was administered with and without ascorbic acid, and the amount of Fe^{59} present in the blood, liver and spleen of the animals was measured three weeks later. In addition, the effect of administering therapeutic iron with milk was investigated as this method is commonly employed in pædiatric practice.

Materials and Methods.

Animals.

Three groups of female albino rats were used. The mean weights ranged between 211 and 236 grammes.

Iron Solution.

An $Fe^{59}Cl_3$ solution (70 μc.) was obtained from the Atomic Energy Research Establishment, Harwell, through the agency of the Commonwealth X-Ray and Radium Laboratory, Melbourne. The solution, which contained 0·33 mg. of elemental iron, was divided into three parts and carrier iron as ferrous sulphate added, so that each part contained 27·6 mg. of elemental iron. The three parts were then treated as follows.

A. The solution was diluted with distilled water to a total volume of 11 ml.

B. Ascorbic acid (150 mg.) was added and the volume made up to 11 ml. with distilled water.

C. The solution was mixed with 6 ml. of milk and distilled water added to 11 ml.

The iron content per millilitre of each solution was therefore 2·51 mg., and there were 13·6 mg. of ascorbic acid per millilitre of solution B.

Experimental Procedure.

One millilitre of solution A was administered by stomach tube to each of the ten rats in the first group. Solutions B and C were similarly administered to the rats in the second and third groups respectively, and an aliquot of each of the three solutions was preserved as a standard. After three weeks the animals were anæsthetized with ether, blood was obtained from the hearts, and the livers and spleens were perfused with physiological saline prior to removal. The radioactivity in the blood and organs was measured on an EKCO scintillation counter as described elsewhere (Brading, Cantrill and Walsh, 1958). The total radioactivity in the liver and spleen was directly measured; that in the circulation was obtained from the radio-assay of the aliquot of blood collected from the heart, and the total blood volume was calculated on the basis of 67 ml. of blood per kilogram of body weight. The percentage of the test dose absorbed was then obtained from these values and from the radioactivity of an aliquot of the administered solution. Any absorbed iron located in organs other than the blood, liver and spleen was ignored.

In the experiments the tagged iron was in the ferric state and the carrier iron in the ferrous state. The results have, however, been calculated without regard to this difference, because it has been shown that in rats both forms of iron are absorbed to about the same extent (Brading, George and Walsh, 1956). It has been assumed that neither form is preferentially absorbed when both are present.

Results.

The results are shown in Table I and Figure I. The mean amount absorbed by the control animals was 30·7 μg., representing 1·2% of the administered dose. A greater amount (58·4 μg.) was absorbed by the animals in the second group, which were given ascorbic acid at the same time as the iron solution. This amount represents 2·3% of the dose and is approximately twice that absorbed by

TABLE I.
Absorption of Iron Administered with Ascorbic Acid or with Milk.

Dose Administered.	Number of Rats.	Mean Weight of Rats. (Grammes.)	Percentage of Dose Absorbed. (Mean.)	Amount Absorbed in Micrograms. (Mean ± Standard Error of Mean.)[1]
(*a*) 2·5 mg. of iron as $FeSO_4$.	9	211	1·2	30·7 ±3·04
(*b*) 2·5 mg. of iron as $FeSO_4$ *plus* 13·6 mg. of ascorbic acid.	10	236	2·3	58·4 ±11·55
(*c*) 2·5 mg. of iron as $FeSO_4$ in milk.	8	220	1·6	40·6 ±8·99

[1] Standard error of mean has been calculated from $\frac{\sigma}{\sqrt{n-1}}$, when n is the number of observations.

the rats in the first group. The difference between the two groups is significant. The mean amount absorbed by the animals in the third group given iron mixed with milk is actually slightly greater than that absorbed by the control animals, but the difference is not significant. The distribution of the absorbed iron between the blood, liver and spleen is approximately the same in all three groups. Between 69% and 75% was found in the blood, between 23% and 30% in the liver and between 1% and 2·5% in the spleen.

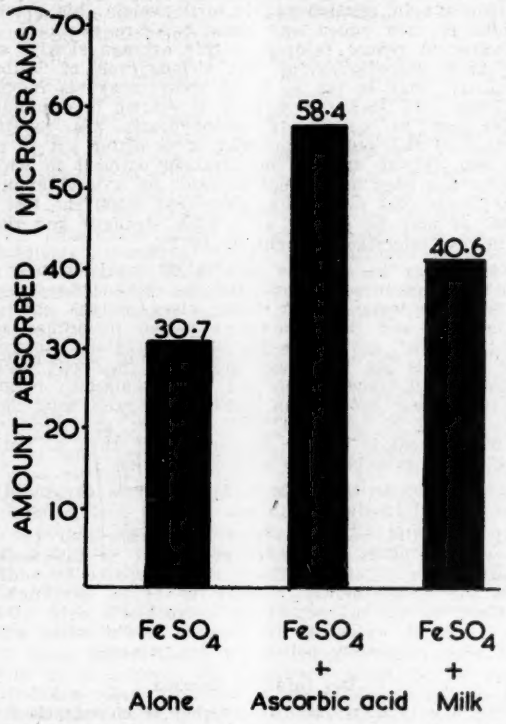

FIGURE I.
The amount of iron absorbed from a test dose of 2·5 mg. of iron given as ferrous sulphate.

Discussion.

The results with ascorbic acid confirm that this substance increases the absorption of ferrous iron into the body. The combination of ascorbic acid with therapeutic iron salts therefore permits increased utilization of iron and enables satisfactory responses to be obtained from doses which are unlikely to produce gastro-intestinal irritation. The results of Moore *et alii* (1939) with human volunteers suggested that ascorbic acid acts by assisting in the reduction of ferric iron and by preventing oxidation of iron already present in the ferrous state. Rats, however, normally absorb ferrous and ferric iron equally well, but in the present experiments it was found that the addition of ascorbic acid increased the absorption of ferrous iron. This raises the possibility that ascorbic acid may have some specific role in facilitating iron absorption independently of its reducing properties.

The results obtained when ferrous sulphate was mixed with milk are interesting because this is a common way of giving iron to infants and young children. It might have been expected that insoluble iron phosphates would have been formed from the phosphates in the milk and that there would have been little or no absorption (Moore *et alii*, 1939). Apparently this reaction did not occur to any significant extent, and there is some evidence that ionized calcium in the food aids iron absorption, possibly by competing with iron inhibitory substances (Anderson, McDonough and Elvehjem, 1940).

One possible objection to the experiment with milk is that the relative proportion of milk to iron was less than that used in practice. If this was important, some reduction of absorption under the experimental conditions might have been expected, whereas a small, although not significant, increase was observed.

Summary.

A solution of ferrous sulphate labelled with Fe^{59} was administered to rats by stomach tube, and the amount absorbed was determined by radio-assay of the blood, liver and spleen three weeks later. The amount absorbed was significantly increased when the iron was administered together with ascorbic acid. The addition of milk to the administered iron solution did not reduce the amount absorbed.

Acknowledgements.

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ECZEMATOUS DERMATOSES OF INFANCY.[1]

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Sydney.

THE eczema syndrome—i.e., erythema with pinhead-sized papules, vesicles, pits, wells and crusts on an erythematous base—is frequently seen in infancy. All too frequently is the condition labelled as "infantile eczema", and no attempt is made to discern the pathogenesis of the eczematous process.

The term "infantile eczema" designates only one of the primary eczematous conditions seen in infancy. It wrongly carries with it a picture of misery to the infant extending into early childhood and adult life. Such a diagnosis should not be lightly made, as the mother, like other members of the family, will be thrown into despair and confusion. Also, unless the child has the dry type of infantile eczema, this state of confusion and despair is not warranted.

By a careful history and examination, with attention directed to the site and the original appearance of the lesions, the family history of the atopic state, the previous treatment and how the rash spread, one can usually place the eczematous eruption under one of the following headings: (1) Those conditions in which the eczema syndrome may be seen as a primary manifestation: (*a*) exudative infantile eczema (not necessarily associated with family atopy); (*b*) dry infantile eczema (neurodermatitis or "atopic eczema", usually associated with family atopy); (*c*) contact dermatitis; (*d*) Orga-

[1] Read at a meeting of the Section of Dermatology, Australasian Medical Congress (B.M.A.), Hobart, March 1 to 7, 1958.

nismal eczematoid dermatitis; (e) drug eruptions. (ii) Those conditions in which the eczema syndrome may be seen as a secondary manifestation: (a) xeroderma; (b) napkin eruption; (c) moniliasis of the skin; (d) seborrhœic dermatitis.

The picture can be confused by the advent of autoeczematization. In this state, the greater part of the body surface of the infant can present the picture of an eczematous dermatitis. Autoeczematization is due to the breakdown of the normal body proteins into various fractions, which act as allergens when absorbed back into the general circulation and delivered to all areas of the body. The eruptions of secondary autoeczematization usually appear on the extensor aspects—i.e., on the fronts of the thighs, over the greater trochanters, on the buttocks, across the shoulders, and on the outer aspects of the arm and the posterior aspect of the forearms as well as the back of the hands.

Exudative Infantile Eczema.

Exudative infantile eczema usually first appears at about seven weeks of age. The young infant is usually fat, pasty, pale and much overweight, the mother will quite proudly tell you that he has already practically, if not actually, doubled his birth weight. These children are usually gluttons, gulping greedily and receiving quickly at each feed far in excess of their requirements for normal development.

The eruption first appears as redness of the flush areas of the face; those are the V of the forehead, the central areas of the cheeks and the chin. These red areas rapidly become exudating plaques and are soon confluent, but usually there is a clear area surrounding the mouth.

If the eruption appears on the rest of the body, it is in the nature of a secondary sensitization rash, and plaques of exudative eczema appear on the extensor aspects of the limbs, on the buttocks and occasionally on the lower part of the abdomen. These also may become extensive and confluent. Becker and Obermayer state that these secondary lesions are toxic in nature, owing to absorption of material (i.e., broken-down protein) from the original lesions on the face.

This type of eruption is usually considered to be due to sensitivity to food. However, as there are persons who authoritatively state that proteins are the sensitizing factor, while others equally incriminate carbohydrates and yet again others fats, I am led to the conclusion that food sensitivity is not known. Ingram states: "... I am convinced, that infantile eczema is never the result of allergic sensitiveness to any foodstuff or to any other specific allergen." Arthur Day believes that this food sensitivity is a quantitative one rather than a qualitative one, and he is in agreement with those people who lay the causative blame on over-feeding. Over-feeding is certainly a factor; I believe that the reason for the development of the rash on the flush areas of the face is similar to that for rosacea. In this latter condition some disturbance of the gastric mucosa leads to flushing of the face on the ingestion of certain foods, notably hot, strong tea and spicy foods. This is a nervous mechanism by way of vagal reflex. My contention is that in exudative infantile eczema there is an inability to deal with a certain constituent of the food—it may be the protein, carbohydrate or fat component for a particular child; this inability to deal with the food causes reflex vagal flushing of the face and increased dilatation of the capillary beds in the dermis, so leading to spongiosis of the epidermis with lysis of the epidermal cells; this in turn causes exudative eczematous patches. On each episode of disturbance of the gastro-intestinal tract, such as occurs with teething, there is a flare-up of the eczematous rash. This condition usually clears with the completion of the two-year-old dentition, never to return again either as asthma or as neurodermatitis disseminata.

In treatment, success has been claimed for taking the child off the breast and giving him all sorts of substitute foods. It is true that in many cases cure has been achieved; but may not the "cure" be due to the fact that in artificial feeding exact food quantities can be measured, and the feedings are under strict supervision by the pædiatrician or mothercraft sister? As an example, goat's milk is hard to get and usually will be supplied only on the request of a medical practitioner—just the sufficient requirement for the day and no more.

The feeds must, however, be regulated, and if possible the baby left on the breast. In addition to all the virtues of breast feeding, a mother feels inadequate and ashamed if she is told that her milk is causing her baby's rash. The child's expected weight is estimated for his age in relation to his birth weight, his present weight is then added and these two are averaged. It is better to reduce feeding to this average slowly, and not do it immediately, as that vicious cycle of "failure to thrive" may be set up if the daily intake is reduced suddenly. To make up volume, if volume is demanded, water can be added. If carbohydrates are required because of the age of the child, it is better not to use the soft, mushy messes, but strained oatmeal to which lactose has been added, not sucrose. As a local application, crude coal tar in zinc paste has stood the test of time. It may be started as a 0·5% strength and then, if that is tolerated, brought up to 1%.

To cleanse the child, a paraffin oil emulsion may be gently rubbed into the paste and the child sponged down with warm water. After being cleansed, the child is patted dry and then allowed a period in diffuse sunlight, to "air" dry before reapplication of the ointment. The skin is an important organ of the body, being concerned in transpiration and heat regulation; because of this never more than one-third of the total body area should be plastered with paste at any one time. If involvement is greater than one-third, then a "Carbowax" water-miscible base should be used.

Because of irritation from fabric fibres, the child is best dressed in linen clothing.

If the child is taken from the breast and put on cow's milk, it is helpful to prepare it in the method suggested by O'Beirne. The milk is prepared by adding, drop by drop (slowly stirring to avoid curdling), a mixture of 2·3 ml. of dilute hydrochloric acid (B.P.) in 7 ml. of water to 0·6 litre of cow's milk, which has been previously boiled for ten minutes.

Dry Infantile Eczema.

The dry type of infantile eczema is characterized by pruritus far greater than the extent of the skin eruptions. These children belong to that group who are designated atopic. Atopy, a term which has undergone many changes of concept since it was first used by Coca, would in the main appear to be a genetic error, transmissible down the line. In this regard it is of interest that, as far as can be ascertained, there have been no atopic phenomena observed in the races of New Guinea (Johnson); yet atopy is a very frequent state amongst the Chinese.

In these people there is an inborn alteration of capacity to react. To trauma they appear to give an acetylcholine rather than a histamine response—a white line on being scratched, not a red one. They also exhibit circulating antibodies to substances with which they have had no contact. They are bright and alert, thin and underweight, and as older infants exhibit a seemingly higher level of intelligence than normal for their age.

The irritability leads to scratching and rubbing; in those areas easily traumatized, excoriated plaques appear—the outer margins of the cheeks from rubbing on the pillow, the sides of the neck, the flexural regions of the elbows and knees and around the ankles.

Fabric fibres and dusts add to the irritation. These are the children who do well away from their home environment, only to relapse on return. When one first examines the child, it is best to examine him in the presence of both parents, one of whom will usually also be atopic. The atopic personality exhibits itself by

emotional tension, and the atopic parent is all over the child. If the mother is the atopic parent, so much the worse. I believe that children do have the power, to a far greater degree than adults, to receive and react to environmental influences. Look at those people who can pick up any child and have him gooing in a matter of seconds! Conversely, look at those who cannot go within ten feet of them without their crying. It is much the same with dogs and horses.

Treatment of these children depends upon reducing the pruritus and ensuring sleep of the baby and the parents. Chloral hydrate for the baby has a dual action—it is in itself an antipruritic as well as a sedative. Phenobarbital can also be used. Phenobarbital for the atopic parent is often helpful.

Locally, if there is much weeping through excoriation and secondary eczematization, wet dressings must be used. When the condition is drier, hydrocortisone in a water-miscible base to calm the skin down is most valuable; there may be absorption of hydrocortisone applied locally (Livingood *et alii*, 1955) and because of this its application should be limited as much as possible. Later, ichthyol and menthol in zinc paste may be applied. Soap is to be avoided; however, some of the tabloid soap substitutes such as "Neutrogena" can be used effectively. Sunshine on the drier eczematous areas is of great value. This may be because of vitamin D production, since calciferol given by mouth to adult patients with atopic eczema is of benefit (Goldberg and Dexter, 1951).

Education of the parents is essential, but difficult. Calm must prevail in the household, and it is essential that only one person inspect and treat the infant. These children, as has been mentioned, are seemingly more intelligent than others of their age group. This intelligence soon becomes diverted to cunning, and much capital by way of cuddling, petting and little walks at night is gained by a good deliberate scratch. In early childhood, food favours, etc., are obtained by carrying on in a tantrum followed by a good scratch if such demands are not met. This condition is the forerunner of the dry neurodermatitis of flexural type in older children and adults. It may be replaced by asthma or hay-fever; these two conditions may alternate in appearance, or unhappily be both present together.

I have hoped that, if the parents can regard their child as a cabbage in a cabbage patch, to be tended with care when attention is essential but left to himself at other times—if they can deal firmly but patiently with the "I get or I scratch" threat—and above all, if they can try to keep the child continuously occupied with some game or toy, and never use food favours as bribes—these children may grow up still having the basic genetic error of atopy, but not its clinical manifestations.

Contact Dermatitis.

Contact dermatitis is frequently seen in infancy, particularly on the exposed areas. Modern plastic toys and fabric toys have dye matter, preservative chemicals, flavouring agents, etc., which can cause allergy. Usually the rash is not symmetrical, as are the two preceding conditions. Medications, applied to cure innocent blotches of the child's skin, or chest rubs, may cause contact dermatitis; once again, the rash is haphazard in distribution. Careful inquiry will usually reveal the cause; the removal of the offending agent and the application of hydrocortisone ointment for two or three days, or of menthol (0·5%) and crude coal tar (0·5%) in zinc ointment for somewhat longer, will produce cure.

Infectious Eczematoid Dermatitis.

The skin surrounding a discharging infected sinus may become eczematous. This is in the nature of a contact dermatitis due to the toxic products liberated by the infecting organism. Curing the infection and using a bland protective ointment on the skin produce satisfactory relief.

Drug Eruptions.

Eczematous drug eruptions may be seen in infants, and here only a careful examination and history may give the answer. I have purposely placed this primary eczematous eruption last, as that is how the diagnosis is usually suspected. If it is not one of the conditions discussed above, one should inquire whether the mother is taking any drugs which could be secreted in the milk, or whether the child is having any medication. Luckily, the condition is rare.

Other Conditions.

There is now to be considered a group of conditions in which the eczema syndrome may be seen as a secondary manifestation.

Xeroderma.

The dry skin of the xerotic infant may be irritated by various chemicals which would not irritate the normal skin; soap, dust, infant toilet preparations, etc., may cause irritation and lead to eczematous dermatitis. This is really a hypersensitivity to these somewhat mild irritants. The lesions are usually seen on the more convex surfaces of the body—those which are easily accessible to the mother's hand holding the cake of soap whilst she is bathing the child—the edges of the lesions tending to fade off into the more normal skin. The use of glycerine cream and superfatted or "Neutrogena" soap usually produces relief. Misdiagnosis and the use of crude coal tar ointment produces disaster: the tar causes irritation and secondary autoeczematization may occur.

Napkin Dermatitis.

Napkin eruptions are caused basically by two factors, the most common being irritation of the skin by chemicals in solution in the urine, the other irritation from the fæces. They are clinically distinct. The chemicals in the urine may be due to faulty protein metabolism by the liver, leading to increased excretion of ammonia, or they may arise externally. One theory is that urea-splitting organisms are present on the skin, which convert urea to ammonia; it is more probable that these organisms multiply rapidly in the warmth of wet napkins with much urea still present, and that they are not properly washed out or killed by adequate washing and boiling, being ready in countless numbers to split urea as soon as the child passes urine. Yet another source is residual alkalinity of the napkin after washing, due to faulty rinsing out of soap. The rash appears as bright erythema on the areas of skin in contact with the napkin, with relative sparing of the creases and folds.

Treatment is first the giving of detailed instructions on napkin washing so that when the napkin is put out to dry it is free from chemicals and sterile. The local application of "Covicone" cream, to which 1% ichthyol may be added, is effective.

The other type, that due to fæces, consists of red maculopapules which show flaccid vesicles on the surface; these readily rupture leaving small ulcerations. These are seen on the buttocks in the area of fæcal contact.

Treatment is directed to a protective application, and some antibiotic incorporated within it. Once again, a silicone-type cream with 2·5 mg. of neomycin per gramme is helpful; but recurrence until the age of about eight months is usually experienced.

Moniliasis of the Skin.

Moniliasis, on the other hand, is seen as bright erythema of the folds and creases spreading up on the convex surfaces. At the border a white collarette of scales is seen, and beyond this there are satellite pustules of a creamy-white colour. "Mycostatin" ointment gives remarkable results in the treatment of this condition. Some infants may experience discomfort when the ointment is applied; this is probably similar to the sensation of burning experienced by some adults on application of "Mycostatin". In these cases "Vioform" in a cream, or

gentian violet (0·13%) in calamine lotion, may be beneficial.

Seborrhœic Dermatitis.

Another condition which may lead to secondary eczematization is seborrhœic dermatitis. This is usually exhibited in the first week of life as a redness of the scalp with some encrusting of adherent brown material. The erythema streams down behind the ears to involve the creases around the neck, onto the eyelids and down into the naso-labial folds. The axillæ, umbilicus and napkin area may also be involved. Occasionally the whole of the trunk becomes erythematous. Usually secondary sensitization will occur with inappropriate treatment. Examination of the scalp of the adults who handle the child will reveal that one at least has a fair degree of dandruff.

Treatment is unsatisfactory, but fortunately spontaneous cure results at about three months, probably owing to the excretion of the excess female hormones absorbed during intrauterine life. First, attention must be directed to the adult scalp, and one of the selenium sulphide shampoos is usually effective. The local application to the baby of "Cetavlon" (2%) and *Liquor Picis Carbonis* (1%) in calamine cream will help to some degree.

Conclusion.

Treatment of each condition has been mentioned only briefly; treatment of the primary condition and of the complications caused by infection is fully set out in standard texts. In my opinion, neither the local nor the internal use of antihistamines has any place in the treatment of the infantile eczemas.

As has been mentioned, owing to absorption of toxic products liberated by the breakdown of epidermal cells, secondary autoeczematization may occur in any of these conditions. This breakdown may occur because of the vigour of the condition itself, or from tissue destruction by inappropriate treatment. A child with autoeczematization in which the original condition may have been "*x*" looks very much like the child whose condition may have been "*y*".

By skin sedation—that is, by the use of simple wet dressings when there is much weeping, and of bland creams containing bismuth carbonate instead of zinc oxide, in case the condition is due to zinc intolerance—the acute state will usually settle and the primary condition be revealed. By careful examination and history taking, the same end may be achieved: however, before the original condition can be treated, the secondary eczematous dermatitis must be soothed.

In my paper I have endeavoured to stress that every infant who exhibits the eczema syndrome may not necessarily have "infantile eczema". Also, yet another theory of the causation of exudative infantile eczema has been advanced; treatment directed along these lines has met with success. Another point that may cause some comment is the belief that exudative infantile eczema is not a manifestation of atopy. I admit that in some atopic children this condition does occur; but in these cases the condition is further complicated, in that there is a mixture of the exudative type and of the neurodermatitis type. Fortunately this is a combination rarely seen, as the atopic child seldom stays still enough for the atopic mother to have the patience to allow him to gorge himself to exudative eczema.

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OXYTOCIN AND OXYTOCIC SUBSTANCE IN BLOOD EXTRACTS BEFORE AND AFTER HYPOTHALAMIC STIMULATION IN RATS.

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Oxytocin and vasopressin are thought to be manufactured in hypothalmic nuclei and to migrate along the axoplasm of axons in the hypothalamico-hypophyseal tract, to be stored in the nerve terminals in the posterior pituitary lobe (Leveque and Scharrer, 1953).

An oxytocic substance (O.S.), which closely resembles, but nevertheless is different from oxytocin has been found in extracts of blood from men, women, sheep, cows, goats and rats (Hawker and Robertson, 1957*a*, 1957*b*, 1958; Hawker and Roberts, 1957; and Duggan and Reed, 1958). This substance (or one closely resembling it) has also been extracted from hypothalami of various species (Robertson and Hawker, 1957). It is possible that O.S. present in blood extracts may be synthesized in sites similar to those producing oxytocin.

Accordingly, it was decided to measure the concentration of O.S. in blood extracts of the rat immediately after electrical excitation of the paraventricular nucleus (on one side) of the hypothalamus, to see whether the release of O.S. into the blood could be stimulated.

Method.

Male Wistar strain rats weighing approximately 250 grammes were anæsthetized with urethane (0·5 gramme given subcutaneously), and a polythene cannula was inserted into the right jugular vein. About 20 minutes later a sample of blood (heparinized) about 1·5 millilitres in volume was collected from each rat through this cannula. The animals were then left in a warm environment for one to two hours.

The Johnson model of the Horsley-Clarke stereotaxic instrument, with a modification of Krieg's coordinates as designed by Duggan and Reed (1958), was used in these experiments.

With the animal orientated in the stereotaxic apparatus, the periosteum was carefully scraped away from the underlying bone and a bore hole was made in the desired position with a dental drill.

A glass electrode was then inserted 7·5 to 8·0 mm. below the surface level of the skull, so that the tip of the electrode was in the region of the paraventricular nucleus on one side. A biphasic stimulus of three volts, with 20 msec. frequency and 12 msec. duration, was then applied for one minute. After this, the electrode was promptly removed and a second blood sample of one or two millilitres was collected through the jugular cannula within one or two minutes.

The blood samples were then extracted and assayed for total oxytocic activity (O.A.), oxytocin and O.S. as previously described (Hawker and Robertson, 1957*a*).

Results.

The results obtained from 22 rats are shown in Table I.

The percentage change in the total oxytocic activity of the blood was estimated in blood taken from 17 rats, and in 15 of these increased oxytocic activity followed stimulation. If the three rats in which there was less than 10% change in activity are excluded, then 12 of the rats showed an increase in total oxytocic activity. In 12 of these 17 rats there was an increase in the level of oxytocin in the blood extracts, in one a decrease was noticed, and in four there was no change. Actually, of 20 rats in this series, oxytocin was elevated in the blood extracts from 15.

In the 17 samples of blood extracts prepared from the same 17 rats, the level of O.S. increased in 10, decreased

TABLE I.

Oxytocic Activity of Acid-Alcohol Extracts of Rat Blood Before and After Hypothalamic Stimulation.[1]

Rat Number.	Oxytocin/Total Activity. (Percentage.)		O.S./Total Activity. (Percentage.)		Percentage Change in Total Activity.	Change in Oxytocin Level.	Percentage Change in O.S. Level.	Oxytocin.[2]		O.S.[2]	
	Before.	After.	Before.	After.				Before.	After.	Before.	After.
1	<60	43·5	>40	56·5			+ 41	<0·51	0·37	0·34	0·48
2	46·75	<48·3	53·25	>51·7			+ 9·8	0·36	<0·42	0·41	0·45
3	>26·2	<45·5	73·8	54·5		+<953%	+ 371	>0·17	<1·8	>0·48	>2·16
4	>53·8	>52·0	46·2	48·0		+ <12·3%	+ 20·4	>0·57	≈0·64	<0·49	<0·59
5	>15·7	>85·5	84·3	64·5		+ 122·7%	− 24·6	>0·22	>0·49	<1·18	<0·89
6	28·4	2·2	71·6	97·8	+ 42·1	− 88·9%	+ 94·1	0·27	0·03	0·68	1·32
7	0	32·8	≈100	67·2	+< 70·4	+ 0·4 mu./ml.[3]	+>7·9	0	0·40	<0·76	0·82
8	0	45·4	100	44·6	+ 71	+ 1·87	− 6·6	0	1·87	2·41	2·25
9	7·5	38·2	92·5	61·8	+> 63·75	+>783·3%	+ 9·5	0·06	>0·50	0·74	0·81
10	2·6	32·5	97·4	67·5	+ 252·6	+ 4250%	+ 143	0·02	0·87	0·74	1·81
11	19·0	20·0	81·0	80·0	+ 60·7	+ 68·75%	+ 58·8	0·16	0·27	0·68	1·08
12	0	25·7	100	74·3	+ 5·7	+ 0·38 mu./ml.[3]	− 22·5	0	0·38	1·42	1·1
13	0	0	100	100	− 22·0	0	+ 64·1	0	0	3·26	5·35
14	0	0	100	100	+ 200	0	+ 66·25	0	0	2·4	3·99
15	30·86	50	69·1	50	+ 2·5	+ 66%	− 25·9	0·50	0·83	1·12	0·83
16	<44·1	22·5	>45·9	77·5	+<444·1	+<215%	+ 756·6	<0·60	1·80	0·76	6·51
17	0	25·4	100	74·6	+ 50·8	+ 0·49 mu./ml.[3]	0	0	0·49	1·44	1·44
18	30·1	54·4	69·9	45·6	+ 7·8	+ 90·9%	− 31·25	0·55	1·05	1·28	0·88
19	33·3	63·0	66·7	37·0	+ 50·8	+ 193·4%	− 43·4	0·61	1·79	1·22	0·69
20[4]	0	0	100	100	+ 148·5	0	+ 51·9	0	0	1·08	1·64
21[4]	0	0	100	100	+ 70	0	+ 22·5	0	0	≈1·20	1·47
22[4]	0	35·9	100	64·1	− 33·8	+ 0·55 mu./ml.[3]	− 60·6	0	0·55	2·49	0·98

[1] "<", less than; ">", greater than; "≤", less than or equal to; "≥", greater than or equal to; "≈", approximately.

[2] *Milliunits per millilitre of blood.*

[3] Milliunits per millilitre; as no oxytocin was present originally, then no percentage change can be calculated.

[4] *Control blood taken one hour after stimulation.*

in six and was unchanged in one. Of 21 animals investigated, there was a rise in O.S. level in 14. However, of these 14 rats, the change in O.S. level *following stimulation was less than 10% in three of* them, so that if these are excluded, then an increase in O.S. was observed in only 11.

In five of the 20 rats investigated there were greater than 10% increases in both oxytocin level and O.S. level; *in 10 rats a rise occurred in oxytocin level and not in* O.S. level; while in five an increase in the concentration of O.S. and not in oxytocin level was observed.

Discussion.

*Olivecrona (1957) has demonstrated that, after electro*lytic lesions of the paraventricular nuclear region in the rat, there is a decrease in the concentration of oxytocin *in the posterior pituitary lobe. Duggan and Reed (1958)* found a decrease in the total oxytocic activity, and in the level of oxytocin and O.S. in extracts of rat blood after similarly placed hypothalamic lesions.

The results obtained in our series show that there is *usually an increase in the total oxytocic activity of the* blood after electrical stimulation of the paraventricular nuclear region, and that this is associated with an elevation in the level of oxytocin in three-quarters of the subjects and of O.S. level in approximately half.

It would appear, therefore, that the paraventricular nuclei in rats are involved in the synthesis of oxytocin, and that, from these observations, no such definite conclusions can be drawn concerning the origin of O.S.

Conclusions.

Extracts of rat blood were investigated for total oxytocic activity, oxytocin and oxytocic substance (O.S.) before and after electrical stimulation of the paraventricular nucleus of the hypothalamus. After excitation *of this region, the total oxytocic activity of the blood* invariably increased. This increase was due to oxytocin and not to O.S.

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Reviews.

A Guide to Orthopædics. By T. T. Stamm, M.B., B.S., *F.R.C.S.; First Edition; 1958. Oxford: Blackwell* Scientific Publications. 8½" × 5½", pp. 115, with 7 plates. Price: 12s. 6d. (English).

THIS little book is an orthopædic gem. The author, who is orthopædic surgeon to Guy's Hospital, has long been known and respected for his clear and often original thinking on many problems, especially disorders of the foot.

In this short volume he has condensed many of his ideas, and expressed them in the lucid way which will be recognized by those who have studied at Guy's during the last 25 years. He makes no attempt to cover the whole subject of orthopædic surgery, and specialized disorders and operative treatment are barely mentioned; but he concentrates on problems such as posture, disorders of the back and feet and the rational use of manipulation, splints and physiotherapy—problems which make up the basic core of all orthopædics. No surgeon could fail to find much that will interest him, and physiotherapists will find here many of their subjects discussed in a most enlightened manner. The book can be recommended strongly to both.

Treatment in Internal Medicine. By Harold Thomas Hyman, M.D.; with a foreword by Walter C. Alvarez, M.D.; 1958. Philadelphia and Montreal: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 10" x 7", pp. 624, with 42 illustrations. Price: £6 17s. 6d.

This is a handsome volume, the excellence of its production being reflected in the cost. The presentation is attractive, and although an eyebrow may be elevated at expressions such as "the overstuffed middle aged man . . ." and "kick the habit", the book is eminently readable.

The conditions dealt with constitute an exhaustive list. In general, diagnostic criteria precede immediate care, continuing care (favourable course), and continuing care (unfavourable course) of the various diseases. There is a valuable supplement on the art of prognosis. Numerous references, mainly from American sources, are given, and a considerable number of tables and figures illustrate the text.

In the sections on diagnostic criteria, emphasis is placed on biochemical data. In some instances it is doubtful whether they warrant inclusion in a textbook of treatment. For example, it is unlikely that the diagnosis of coronary artery occlusion will be influenced by the levels of lactic and malic dehydrogenase, zinc, glucose isomerase or copper.

A number of drugs are mentioned which are not generally available in this country, and proprietary drugs have, not uncommonly, different names in America from those used in Australia. Corticosteroids and corticotrophins are advocated for a wider range of conditions than is customary in British medicine. Although, in general, accepted techniques are suggested, many clinicians would not agree with the strong support given to stellate ganglion block in cerebral artery occlusion.

A more basic—and cheaper—textbook of treatment would fulfil undergraduate requirements. The post-graduate can keep abreast of therapeutic advances by reading the periodical literature. The senior reader, however, will find in this book a readable account of current medical therapy in the United States of America.

Advances in Tuberculosis Research. Edited by H. Birkhäuser, H. Bloch and G. Canetti; Volume IX; 1958. Basel and New York: S. Karger. 9½" x 6½", pp. 350, with 69 figures and 30 tables. Price: sFr. 64.

THE ninth volume in this series commences with a paper by Esmond R. Long on "Tuberculosis in Our Time". He is of the opinion that the low death rate in females "and the present preponderance of tuberculosis in the late years of life are the two most important facts in the demography of tuberculosis today". Although some departments of health are "convinced that tuberculosis is on the way out", Long notes with approval that "many good medical schools have expanded rather than contracted their education in tuberculosis".

In his article on "The Pathogenesis of Tuberculous Cavities", Yuichi Yamamura, of Kyushu University, Fukuoka, states that it has been proved that allergy plays a major part in cavity formation. Because successful desensitization in animals prevented cavity formation, Yamamura is hopeful that "these experimental results may be suggestive for the treatment and prevention of tuberculous cavities in human subjects".

Professor V. I. Pusik and Dr. O. A. Uranova, of the Academy of Medical Sciences, Moscow, report on studies of "Patho-Histological Changes in the Nervous System in Various Forms of Tuberculosis in Man". Their investigations have shown that different forms of tuberculosis of the lungs and of the lymphatic system produce characteristic changes in the nervous system, and that these vary with the type of tuberculosis—e.g., acute primary, hæmatogenous and chronic fibrocaseous types of the disease.

In order to study the relationship between lymphogranulomatosis benigna (Boeck-Schaumann syndrome) and atypical tuberculosis (Ziegler), Lennert Zettergren of Gothenberg conducted a histo-pathological investigation. He divided his material into two series. In the first series were 59 lymph nodes in which tubercle bacilli were found—Ziegler's large-celled hyperplasia. In the second series were 53 lymph nodes in which no bacilli were found; they came from patients with the clinical features of lymphogranulomatosis benigna. Histologically the two series showed great similarity, and the author supports the view that lymphogranulomatosis benigna is a tuberculous disease, and in his opinion the Ziegler form of tuberculosis is a transitional form between classical tuberculosis and lymphogranulomatosis benigna.

In an article on methods of testing chemotherapeutic and antibiotic substances in experimental mouse tuberculosis, W. H. Wagner of Frankfurt gives several reasons why the mouse is useful in such experiments. He states that experimental tuberculosis in the mouse is mainly acute, and is localized to the lungs. Spontaneous infection is rare, whereas multiplication of bacilli is more rapid in the lungs of a mouse than in man or guinea-pig. Histopathological manifestations can be well defined. Mice are inexpensive and they multiply rapidly. Only small amounts of substances to be tested are required. The author also observes that certain strains of tubercle bacilli—e.g., INH-resistant mutants—are virulent for mice only, and not for guinea-pigs. Wagner recommends that therapeutic substances which act favourably in mice should be checked in other experimental animals, as certain drugs act in guinea-pigs and not in mice, and vice-versa. He regards the mouse as the most valuable experimental animal for testing the chemotherapy of tuberculosis.

Dr. B. Kreis of Paris discusses the enzyme deficiencies of isoniazid-resistant strains of tubercle bacilli. Kreis states that the knowledge of these enzyme deficiencies would remain of academic interest only if they did not help to explain the pathogenic action of the bacilli. One factor alone cannot adequately explain the specific action of INH on sensitive bacilli and its lack of action on resistant bacilli. He thinks that the "regressive action" of these bacilli in the animal, as well as the differences observed in experimental disease and human disease due to these bacilli, can be explained by the elimination of the destructive products of hydrogen peroxide in the lesions. The action of INH can be explained by a chain of enzymatic reactions which is blocked at a certain point in resistant bacilli.

"The Use of Radio-Active Isotopes in the Study of Experimental Tuberculosis" is discussed by Joseph Sternberg of Montreal. Since this is a relatively new field, he warns that "there are many difficulties and pitfalls". Both bacilli and drugs can be labelled. He thinks that this research can lead, amongst other things, to a better understanding of the action of antituberculosis drugs and antibiotics and "give information about the biochemical exchanges between the labelled bacillus and the infected host".

The papers in this volume are well illustrated, and each is accompanied by an extensive bibliography. The reproductions of the photographs of histopathological specimens are excellent. These papers should be read by everyone interested in research in tuberculosis.

The New Chemotherapy in Mental Illness: The History, Pharmacology and Clinical Experiences with Rauwolfia, Phenothiazine, Azacyclonol, Mephenesin, Hydroxyzine and Benactyzine Preparations. Edited by Hirsch L. Gordon, M.D., Ph.D., F.A.P.A.; 1958. London: Peter Owen Limited. 9" x 5½", pp. 785, with many illustrations. Price: £6 1s.

THE editor has selected from various medical journals a miscellany of articles (by many well-known American psychiatrists) which were published between 1954 and 1957. Some of these articles were most stimulating when they appeared, and the book under review gives the reader a comprehensive background to the early developmental phase of tranquillizing drugs and thymoleptics. The fact that with one exception the authors are American naturally gives a rather one-sided presentation of the results achieved in the use of these drugs. The editor himself has written an interesting historical survey of the drugs under discussion as an introduction, but this contains many inaccuracies in nomenclature which are confusing to one unfamiliar with their usage. The chief drawback to such a book is, of course, that by the time that it becomes available, so many advances have been made and so many new drugs have been discovered that the publisher's claim

that it "provides the only completely comprehensive survey of the latest advances in chemotherapy in mental illness" loses much of its value.

However, it is a very convenient means of having the opinions and findings of many different psychiatrists readily available, especially as the whole field of the use of drugs in mental illness is becoming increasingly diverse year by year. Thus, the main advantage of this book is that it provides a broad foundation upon which can be built a knowledge of the more recent advances in this area of psychiatric endeavour. A regrettable omission is that there is no index or system of cross reference in the book.

Clinical Orthopædics. Anthony F. DePalma, Editor-in-Chief, with the assistance of the Associate Editors; The Board of Advisory Editors and The Board of Corresponding Editors. Number Twelve; Fall, 1958. Philadelphia and Montreal: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 10″ × 7″, pp. 340, with many illustrations. Price: 82s. 6d.

THIS is the twelfth of a series of volumes in symposium form prepared under the auspices of the Association of Bone and Joint Surgeons. It is concerned primarily, but not exclusively, with problems of rehabilitation.

There are 12 articles by various authors on different aspects of rehabilitation, and these cover 168 pages. A few papers are clear and authoritative—for example, an excellent review of rehabilitation of the amputee by Henry Kessler. Other contributions tend to be either hackneyed and repetitive or confined to very specialized problems. It is a symposium merely in the sense that many facets of rehabiliation are discussed.

The second half of the book is devoted to a variety of orthopædic problems, varying from mundane fractures to osteoarthritis of the hip in a gorilla. Here again, the standard of the contributions varies greatly, and there is undue stress on hip prostheses and new methods of metal fixation of femoral fractures—a common feature of American orthopædic publications.

This publication can have only a very limited appeal to Australian surgeons. It is neither a textbook nor a scientific journal. To purchase all the volumes of "Clinical Orthopædics" (and there are more still to come) would give a reader a very expensive and modern reference library on most orthopædic problems; but the best reviews and research work are published in the *Journal of Bone and Joint Surgery*. There are six large issues of this journal from America every year, and there must be very little that is worthwhile that escapes its pages.

The Year Book of Pediatrics (1958-1959 Year Book Series). Edited by Sydney S. Gellis, M.D.; 1958. Chicago: The Year Book Publishers. Melbourne: W. Ramsay (Surgical), Limited. 7¾″ × 5″, pp. 496, with 123 illustrations and four tables. Price: 82s. 6d.

THE editor, Sydney S. Gellis, has done another excellent piece of work in this "Year Book". We found particularly interesting the section on staphylococcal infections in newborn infants, a subject which has been occupying the anxious attention of all concerned with obstetrics and pædiatrics for some time. Dr. Gellis, finding a state of confusion induced by the many papers on this matter written from differing points of view, asked Dr. Richard T. Smith "to prepare a practical outline based on presently available information to guide physicians in controlling spread of the staphylococcus and in handling an outbreak of infection". This "outline" is printed in full, and may be recommended to the attention of all those interested.

This "Year Book" is full of interest, to which the editor's comments contribute not a little. Its immediate sphere of reference is the specialist pædiatrician; but it could be very useful to all practitioners concerned with the problems of childhood.

Clinical Neurosurgery: Proceedings of the Congress of Neurological Surgeons, Washington, D.C., 1957; Volume V. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9″ × 5¾″, pp. 226, with many illustrations. Price: 88s.

THIS book is the fifth of a series; it contains the proceedings of the seventh annual meeting of the American Congress of Neurological Surgeons in 1957. On this occasion Dr. Francis Grant of Philadelphia has been honoured and is the principal contributor. First Dr. Grant presents some of the results of his long experience in three excellent papers. These deal with posterior fossa gliomas in children, basal meningiomas and cordotomy.

The rest of the book is concerned with problems particularly associated with neurosurgery in children. Two papers are of special interest. The first, by Pudenz, on ventriculo-atrial shunting of cerebro-spinal fluid into the circulatory system, is important because the procedure appears to offer good prospects for treatment in some cases of communicating hydrocephalus. The second, by Irvine Cooper and Bravo, is on chemopallidectomy in the alleviation of the involuntary movements of dystonia musculorum deformans and other movement disorders of childhood.

Some very good material has been collected in this book, which would interest all neurosurgeons, but would be of greatest value to those concerned with neurosurgical conditions in childhood.

Principles of Radiographic Exposure and Processing. By Arthur W. Fuchs; 1958. Oxford: Blackwell Scientific Publications. 9¼″ × 7″, pp. 304, with 159 illustrations. Price: 80s. (English).

THIS book is a fund of useful information. There is nothing new in its subject matter, but all principles are correctly stated and elaborated. Physical concepts are treated sketchily and superficially. By contrast, the introduction of such terms as "ectomorphic" in the discussion of body types appears ill-balanced. An unusual and informative section is provided on the details of the manufacture of X-ray film, and the description of the process of image formation is more lucid and complete than is usual.

The advantages of high kilovoltage techniques are stressed in the reproduction of the total anatomical detail in long-range contrast with short exposure time and minimal irradiation of the patient. Further, a wider exposure latitude is permitted with the production of radiographs of acceptable density and contrast. Standardization of exposure factors is recommended, such that when the optimal kilovoltage for a part is determined, the only variable should be the milliampere-seconds, according as the part is within the small, average or large range of thickness. A useful graphic illustration of the influence of the anode "heel" effect is provided, and the advantage to which this may be used in rendering uniform the radiographic density of parts of unequal thickness is illustrated.

The section on processing procedures is current and comprehensive. Means of minimizing the deleterious effects of processing at high temperatures are suggested, and details of processing methods to allow rapid viewing of the radiograph in the surgical management of a patient are provided.

Insufficient emphasis has been placed on the necessity for and means of protection of the patient and of the technician.

In view of the difficulty in reproducing radiographs and of the fine distinctions of quality attempted, the illustrations are superb. The methods of experimental proof of statements advanced are simple and ingenious. The text is enlivened by an account of the historical background of the various technological advances. A glossary is appended, as is a list of references for further reading. Unfortunately, typographical errors in the text and tabulations, careless construction and syntax, laboured and redundant exemplifications, repetition and "padding" often make the reading tedious.

This book will provide most useful refreshment for a qualified technician, but cannot be recommended as an introduction to radiography for student radiographers in Australia, as the treatment of certain aspects is too superficial to satisfy their qualification requirements.

Gynecologic Radiography. By Jean Dalsace, M.D., and J. Garcia-Calderon, M.D.; with a chapter on "Radiography of the Breast", by Charles M. Gros, M.D., and Robert Sigrist, M.D.; Foreword by I. C. Rubin, M.D.; 1959. New York: A Hoeber-Harper Book. 9¼″ × 6½″, pp. 208, with 305 illustrations. Price: $8.00.

THIS publication is a work for the specialist. It is compiled rather like an atlas, and the reproductions are extremely good, even those of films taken many years ago.

The authors have traced the history of the usage of opaque media in the investigation of the uterus and Fallopian tubes from its inception. They admit that the method has at times met with criticism, particularly in the examination of the body of the uterus, but postulate that it has a great field and is of great diagnostic value.

There is little new material in the information as to technique, but it covers the methods of administration

fully, and deals with faults in technique and those hazards which may beset the unwary.

The appearances of the normal and of congenital malformations are well described. There is also a chapter on carcinoma both of the uterus and of the cervix. It is in relation to this examination that there are both criticism and disapproval of the method. Some writers believe that the risks and, to them, lack of definite information do not justify its undertaking. However, the writers make a very good case and are very convincing.

In general, the impression gained of this book is one of painstaking work which has been presented in a very attractive form.

Lecture Notes on Midwifery. By T. F. Redman, T.D., M.B., Ch.B., F.R.C.S. (Edin.), M.R.C.O.G.; 1958. Bristol: John Wright and Sons, Limited. 7¾" × 4¾", pp. 220. Price: 12s. 6d. (English).

THIS handbook is planned to provide a lecture summary for pupil midwives. The author is a product of the Manchester school, and pays tribute to that great teacher the late Professor Daniel Dougal, whose style has been followed, the result being wonderfully clear lecture notes.

The well-considered use of seven different types makes the subject matter literally leap from the page.

The composition is fresh and original, and the teaching modern. Old teachings, which have throughout the years been copied from one textbook to another although proved fallacious, have no place in these notes. It is refreshing to see in print that incarceration of the retroflexed gravid uterus is very rare, and that retrodisplacement is found in 20% of the population and there is little justification for correcting it.

Although the choice of subjects is limited to those required in the teaching of midwives, many of the sections —notably those on ante-partum hæmorrhage, the Rhesus factor, thromboembolic phenomena and prolonged labour— are useful résumés of the latest advances in these subjects. The chapter on preeclampsia is especially good, and in the prevention of eclampsia the teaching is along the lines of the Australian work. Relevant reference is made to the history of obstetrics—for example, "1910—the first antenatal clinic opened in Adelaide by Wilson"—and in the chapter on the management of the puerperium the reader is reminded that Charles White of Manchester in 1772 advocated "early rising" in the puerperium.

The author, though keeping to his modest aim of providing lecture notes for midwives, has produced a small, inexpensive, ready-reference practical handbook, the reading of which will reward any practitioner of obstetrics.

Diseases of Livestock. By T. G. Hungerford, B.V.Sc., H.D.A.; Fourth Edition; 1959. Sydney, Melbourne, Wellington and London: Angus and Robertson, Limited. 9¼" × 5½", pp. 624, with many illustrations. Price: 80s.

THIS is the fourth edition of a book which already has no rival as a quick source of information on all of the diseases affecting livestock, other than poultry, in New South Wales. "Diseases of Livestock" has obvious limitations; these are described quite frankly in the introduction, and the author has maintained a consistent standard without attempting to go beyond them. The book is designed primarily for farmers and others directly concerned with animals, and 474 pages cover the actual diseases of seven animal species at an appropriate level. This section has some value for veterinary surgeons, because of its comprehensiveness and the differential diagnostic charts which it contains.

A brief early section gives relevant details and procedures of animal husbandry, such as gestation periods, and methods of administering medicines and disposing of carcasses. The general discussion of diseases is followed by a chapter on poisons, including poisonous plants, and a chapter on the zoonoses. Next comes a set of appendices dealing with eight groups of drugs—for example, anthelmintics and preparations for treating infected eyes. Finally, there is a "Veterinary Physician's Index". This is the one chapter intended for professional people, and they should find it very useful in the selection and location of pharmaceutical preparations. The book has an adequate index.

There are some technical deficiencies. There are very few references given, so that the book has practically no value as a guide for further reading. This is a pity, since there is no other single book dealing with all the livestock diseases in the whole or any part of Australia. There are also some sections which are out of date. Mycotic dermatitis of sheep, for example, is described as an infection by a dust-borne fungus. It is actually caused by a bacterium which apparently requires fairly direct transmission.

Mr. Hungerford is an experienced rural veterinary practitioner, and he thoroughly understands the needs and difficulties of animal husbandmen when confronted with disease problems. It would, however, be tragic if this book was to persuade such people that they could be independent of professional advice and assistance.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Basic Physics in Radiology", by L. A. W. Kemp, B.Sc., Ph.D., F.Inst.P., and R. Oliver, M.Sc., F.Inst.P., A.M.I.E.E.; 1959. Oxford: Blackwell Scientific Publications. 8¾" × 5½", pp. 343, with 143 illustrations. Price: 35s. (English).

Written to provide, within the limitations of a single volume, a reasonably concise treatment of the basic physics background of medical radiology.

"Anatomy of the Human Body", by R. D. Lockhart, M.D., Ch.M., F.R.S.E., G. F. Hamilton, B.Sc., M.B., Ch.B., and F. W. Fyfe, M.A., M.B., Ch.B.; 1959. London: Faber and Faber, Limited. 9¾" × 7", pp. 708, with 965 illustrations. Price: £5 5s. (English).

The authors state simply: "To lighten the burden of the student of anatomy is the purpose of this book".

"The Psychiatric Aide: A Textbook of Patient Care", by Alice M. Robinson, R.N., M.S., foreword by Walter E. Barton; Second Edition; 1959. Philadelphia and Montreal: J. B. Lippincott Company. Sydney: Angus & Robertson, Limited. 8" × 5", pp. 226, with illustrations. Price: £1 18s. 6d.

This book is addressed "not only to the psychiatric aide but also to students of nursing, teachers, interested laymen and all others whose endeavors are directed toward helping those unfortunate persons who have lost their way".

"The Effect of Pharmacologic Agents on the Nervous System", Research Publications, Association for Research in Nervous and Mental Disease, Volume 37; edited by Francis J. Braceland, M.D.; 1959. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5¾", pp. 502, with 124 illustrations and 34 tables. Price: £7 8s. 6d.

Proceedings of the meeting of the Association for Research in Nervous and in Mental Disease, December 13 and 14, 1957, New York.

"Speech and Brain-Mechanisms", by Wilder Penfield and Lamar Roberts; 1959. Princeton and New Jersey: Princeton University Press. 9¼" × 5¾", pp. 304, with many illustrations. Price: $6.00.

The outcome of ten years' study of brain dominance, and of aphasia and other speech disturbance . . . "a discussion of the cerebral mechanisms of speech, the learning of language and the teaching of language".

"Pathology", by Peter A. Herbut, M.D.; Second Edition; 1959. Philadelphia: Lea & Febiger. Sydney: Angus & Robertson, Ltd. 10" × 8½", pp. 1516, with 758 illustrations. Price: £10 3s. 6d.

The author and most of his collaborators are connected with the Jefferson Medical College, Philadelphia, Pennsylvania.

"The Practical Evaluation of Surgical Heart Disease" (The Glover Clinic), written and compiled by Robert G. Trout, M.D., edited by Robert P. Glover, M.D.; 1959. New York, Toronto and London: McGraw-Hill Book Company, Inc. 11" × 8½", pp. 143, with 44 illustrations. Price not stated.

" . . . a rather drastic simplification of the subject relying purely on fundamentals which have proved themselves by extensive clinical application to serve more adequately this book's intended purpose as a guide and general reference."

The Medical Journal of Australia

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KURU.

THE first medical description of kuru, by V. Zigas and D. C. Gajdusek, appeared almost simultaneously in this journal[1] and in America[2] towards the end of 1957. We then predicted[3] that the problem of this unusual condition amongst the Fore people of New Guinea would intrigue the medical world and that the results of further investigations would be awaited with much interest. In their earliest reports Zigas and Gajdusek described 150 cases of kuru observed in various parts of the area. The disease had been found only among the Fore and in closely adjoining parts of some neighbouring tribal areas. The clinical picture was described as resembling paralysis agitans and the course of the disease as being "unrelentingly progressive with continuous and uninterrupted deterioration". The age incidence ranged from four years to late adult life, and the sex incidence was described as being predominantly female, two-third of the cases occurring before puberty being in girls, and the adult cases being almost wholly in females. The results of an extensive list of laboratory investigations were reported, all essentially negative. A wide variety of therapeutic agents had been tried empirically without apparent effect on the course of the disease. At this time, Zigas and Gajdusek said that their investigation had failed to reveal any aspect of the Fore dietary, social or geographical situation which might indicate an environmental factor responsible for the condition, and they stated that a "genetic predisposition" must be considered.

In the early part of 1958, a small group from the University of Adelaide conducted investigations in the area, and their findings were reported later that year[4] and at the beginning of this year.[5,6] On the clinical aspect, D. A. Simpson, H. Lander and H. N. Robson[5] described a detailed neurological study of 27 cases. They considered that the neurological signs were those of a progressive, ultimately very gross motor incoordination suggesting cerebellar dysfunction. Increase of passive tone of extrapyramidal type was not constantly present. Mental changes, mainly of affect, were prominent. No sensory disturbance could be demonstrated. They confirmed that the pattern and course of the disease were strikingly uniform, but found that the rate of deterioration was not always even. They did not agree with the statement of Zigas and Gajdusek that the disease resembled paralysis agitans. The pathological features of five cases studied were described by M. Fowler and Graeme Robertson.[6] They reported that there was widespread neuronal atrophy, especially in the cerebellar cortex (mainly the vermis and the flocculo-nodular lobe). Other structures involved included the dentate nucleus, thalamus, corpus striatum, globus pallidus and parts of the cerebral cortex (particularly the anterior central gyrus). In the spinal cord, degeneration of spino-cerebellar and lateral cortico-spinal tracts was found. Most of the cranial nerve nuclei were spared, and the substantia nigra was only slightly involved. No evidence was found of an infective cause of the pathological features, and it was considered that the appearances most resembled some toxic or degenerative process. A further study of 15 cases was presented by Klatzo, Gajdusek and Zigas[7] before the American Association of Neuropathologists this year. More detailed information on this large collection of material has just been published,[8] and this should provide a valuable opportunity for clinico-pathological correlation. The findings appeared to be very similar to those described above, and again no particular ætiological factor could be strongly incriminated.

In their later reports[9,10] Gajdusek and Zigas have extended their observed series to some 200 cases. They reaffirm their belief that kuru occurs only among the Fore and in those neighbouring tribes which have a tradition of intermarriage with the Fore, and again describe the wide range of environmental and laboratory investigations which they conducted with largely negative results. However, despite the generally negative nature of the results of such studies so far, there would seem to be a number of leads which well deserve closer study. The suggestion that pregnancy may temporarily retard the progression of the disease and that rapid deterioration occurs during the puerperium may point to an endocrine influence on the disease. Although extensive trace metal analyses have been performed, the search does not appear to have covered all possible metallic elements. The finding[10] by Curtain of gross elevation of both beta and alpha serum globulins merits further study, possibly combined with more detailed and extensive investigation of urine amino-acid content than appears to have been done so far.

Perhaps the most arresting development in the investigation of this disease to date is the suggestion[4,11] by J. H. Bennett, F. A. Rhodes and H. N. Robson that the disease may well be genetically determined. This is based on the results of a genealogical survey carried out in the North Fore area in which pedigrees were constructed comprising some 2000 individuals. Kuru

[1] MED. J. AUST., 1957, 2: 745 (November 23).
[2] *New Engl. J. Med.*, 1957, 257: 974 (November 14).
[3] MED. J. AUST., 1957, 2: 765 (November 23).
[4] *Aust. Ann. Med.*, 1958, 7: 269 (November).
[5] *Aust. Ann. Med.*, 1959, 8: 8 (February).
[6] *Aust. Ann. Med.*, 1959, 8: 16 (February).
[7] *J. Neuropath. exp. Neurol.*, 1959, 18: 335.
[8] *Lab. Invest.*, 1959, 8: 799.
[9] *Klin. Wschr.*, 1958, 36: 445.
[10] *Amer. J. Med.*, 1959, 26: 442 (March).
[11] *Am. J. hum. Genet.*, 1959, 2: 169.

was stated to be the cause of death in 204 instances, including 177 females (21 children) and 27 males (19 children). Analysis of these data showed that male victims of kuru were born almost exclusively to mothers who themselves later died of the disease and that there was a similar association between young female victims and their mothers. The incidence of kuru in this material was found to be almost equal in young males and in young females, while adult males were rarely affected. Bennett and his colleagues suggested that these findings could be explained by the hypothesis that the disease was controlled by a single autosomal gene (*Ku*) which was recessive to its allelomorph (*ku*) in males and dominant in females. Individuals who were homozygous (*KuKu*) were presumed to have an early onset of the disease, while the heterozygote situation (*Kuku*) would produce the late onset type of the condition in females. These studies were reported as being preliminary, and the genetical hypothesis was advanced in a tentative manner. Early this year, however, work commenced, supported by the University of Adelaide and the Public Health Department of the Territory, to extend these genealogical studies considerably and to obtain more data in order to test this genetical hypothesis. Results of this work to date are reported in this issue by J. H. Bennett, A. J. Gray and C. O. Auricht (see page 505). The material has now been extended to include the records of over 5000 individuals, and it is of major interest to note that the same striking family patterns have been consistently found. This confirmation lends very strong support to the genetical interpretation previously advanced,[4] particularly when viewed against the background of the completely negative nature of the results of environmental investigations so far and many of the epidemiological features which have been reported.[10]

The present situation would therefore seem to be that the evidence so far most strongly favours a genetical basis for this disease. In this event, the very high frequency of this condition amongst the Fore people presents an almost unique and challenging problem in human genetics, which will require most careful and possibly prolonged study. The genetical theory, moreover, immediately provides a basis from which a number of lines of further enquiry stem, and may well represent the first important step towards the identification of the defect responsible for this strange and terrible disease.

Current Comment.

FIBROCYSTIC DISEASE OF THE PANCREAS AND ADULT EMPHYSEMA.

Modern treatment has transformed the outlook for many children with fibrocystic disease of the pancreas; perhaps the most important single factor in reducing mortality and morbidity has been the continuous use of antibiotics such as tetracycline over long periods. As a result, adolescents and, indeed, young adults with the fully developed condition are no longer rare. It may well be this observation which has stimulated the search in certain quarters for unrecognized cases of the disease among emphysematous adults; a possible example was recently investigated by B. Marks and Charlotte Anderson.[1] J. A. Wood and his colleagues,[2] who include Paul di Sant'Agnese, have studied pulmonary and pancreatic function, together with sweat chloride concentrations, in a series of emphysematous subjects. Five of 24 such patients were found to have abnormally high levels of chloride in the sweat (an almost constant finding in fibrocystic disease). Four of these subjects showed evidence of impaired absorption of neutral fat, suggesting decreased pancreatic activity, although duodenal trypsin and serum vitamin A levels were within the normal range. Three of them also had low serum carotene concentrations, but this was found in four out of five emphysematous patients, with normal findings from sweat tests, in whom this estimation was made. The authors also report abnormal findings from sweat tests in five of 36 parents of children with fibrocystic disease. In three of these subjects the maximum breathing capacity was somewhat lower than expected, but it was also reduced in four parents with normal findings from sweat tests. Studies of pancreatic function in this series are not described; indeed a weakness of the whole investigation lies in the fact that all the tests were not done on all subjects, so that the significance of some of the findings is difficult to assess. The authors justifiably observe that the four emphysematous subjects may represent *formes frustes* of fibrocystic disease, but this is not necessarily true. Such a conclusion rests largely on the finding of abnormally high chloride concentrations in the sweat, and it is desirable to know more about this phenomenon before it can be used in adults, with or without pulmonary disease, as the diagnostic test which it virtually is in childhood. Nonetheless, on other evidence, as well as that produced by Wood and his co-authors, the existence of "incomplete" examples of fibrocystic disease may reasonably be assumed. Search for and studies of these cases may well throw some light on the ætiology of chronic bronchitis and emphysema in adults.

THE TREATMENT OF BLOOD CHOLESTEROL LEVELS.

In view of the current widespread interest in the possible association between certain dietary factors and heart disease, as evidenced by statements in the daily Press, discussions in medical literature, and even questions in Parliament, the comments on safflower oil made by the Council on Drugs of the American Medical Association[3] are of considerable topical interest. The Council states that safflower oil is a natural substance (extracted from the seeds of the safflower, *Carthamus tinctorius*) which is very rich in linoleic acid, an essential unsaturated fatty acid. The effect of certain unsaturated fatty acids in lowering the serum cholesterol levels of individuals suffering from hypercholesterolæmia, when taken in sufficient quantities, has been the subject of a number of recent reports. However, the Council points out that safflower oil does not lower serum cholesterol levels to any appreciable extent unless it is substituted for saturated fatty acids already in the diet; to achieve the maximum effect, it is necessary that food fatty acids should be present in the ratio of approximately three parts of unsaturated fatty acids to one part of saturated fatty acids. This means that the hypercholesterolæmic subject who wishes to effect any substantial reduction in his serum cholesterol level must ingest large amounts of unsaturated fatty acids, while drastically reducing his intake of animal fats. It should be noted that a change to a diet high in unsaturated fatty acids has little or no effect on the serum cholesterol level in individuals in whom this level is normal.

The therapeutic use of safflower or other vegetable oils with a high content of unsaturated fatty acids derives from observations of the statistical relation which has

[1] Med. J. Aust., 1959, 2:160 (August 1).
[2] *New Engl. J. Med.*, 1959, 260:951 (May 7).
[3] *J. Amer. med. Ass.*, 1959, 169:2019 (April 25).

been shown to exist between raised cholesterol levels and arteriosclerotic disease. The Council on Drugs remarks that the fact that there is a statistical relationship between two variables does not prove that one causes the other, but that it yet seems reasonable to postulate that a sustained reduction in blood cholesterol levels may be desirable for those in whom the level is raised. However, it is noted that whether safflower oil or any other cholesterol-level lowering agent has any effect, good or bad, on the over-all physical status of the patient remains to be proved, and that the clinical use of such substances must therefore be considered experimental. The Council reminds its audience that the proposed daily dose of safflower oil provides about 450 Calories, so that, if it is taken without a corresponding reduction in the usual diet, weight gain may be expected. It is pointed out that obesity is commonly associated with elevated cholesterol levels, and that hypercholesterolæmia may often be improved by simple weight reduction. Finally it is stated that, apart from a slight tendency to cause diarrhœa, safflower oil is notably free from side-effects; however, like other fats it is a cholecystagogue, and should be used with caution in patients with gall-bladder disease.

LEPROSY.

New data on the way in which leprosy is spread were brought out at discussions by the WHO Second Expert Committee on Leprosy, recently concluded in Geneva. It was shown that definite susceptibility to leprosy exists, since not everyone in close contact with the patient is likely to contract the disease. For example, conjugal leprosy is very rare. Moreover, children, who make up the most vulnerable age-group, often do not get leprosy from parents who are sufferers. In order to contract the disease, which is less contagious than tuberculosis and most other common infections, special susceptibility is necessary in healthy individuals. On the other hand, resistance to leprosy can be acquired and detected. Persons with this resistance contract the disease only in a mild form. The members of the Committee recommended that leprosy campaigns now under way be followed up and extended by the use of ambulatory treatment with sulphones. Ambulatory care is, in fact, the only valid method of dealing with the problem, since there are about 12,000,000 leprosy sufferers in the world, mostly in tropical and equatorial countries, and not more than 100,000 of them can be hospitalized in existing institutions. There are 1,500,000 persons already receiving treatment while remaining with their families, and it is hoped to increase this number greatly in the near future.

The Committee gave some attention to the question of deformities caused by leprosy, pointing out that they can be prevented by early treatment, that incipient deformities can be prevented by teaching the patient how to care for his hands and feet, and that many deformities can be corrected by physiotherapy and plastic surgery. The legislation that exists in some countries, requiring that leprosy patients be segregated, also was discussed. Such legislation, it was felt, should be abolished in view of the relatively low infectivity of leprosy, which should be dealt with as an ordinary public health problem in the same manner as other communicable diseases.

THE WELFARE OF CHILDREN IN HOSPITAL.

So long as children are admitted to hospitals, so long will the hardy perennial of their welfare in hospital be before us, to some a challenge, to some a tiresome bother, to some a nugacity. It appears to be a topic which has in the past engendered, and continues to engender, much more interest in England than in Australia, although through these pages we have from time to time endeavoured to widen and deepen the interest of hospital authorities, doctors and nurses in this subject.[1] It is noteworthy that numerous references have appeared in the British lay Press, as well as frequent articles and much correspondence in medical journals, and now we have to hand "The Welfare of Children in Hospital",[2] a report to the Central Health Services Council of the Ministry of Health, prepared by a committee representative of the medical and nursing professions, hospital administration and almoners which met under the chairmanship of Sir Harry Platt, the President of the Royal College of Surgeons. The terms of reference of the committee were to study the arrangements in hospitals for the welfare of ill children, as distinct from their medical and nursing treatment. This is a great advance upon the concept that a child in hospital was there to be treated for some condition, the medical and nursing considerations were paramount, and any suggestion of welfare was to be scouted as certainly likely to interfere with the service of doctors and the ministrations of nurses.

It must be gratifying to those interested in the whole child, sick or well, to read that the members of the committee were "unanimous in our opinion that the emotional needs of a child in hospital require constant consideration". Due recognition is given to the possible harmful effects of separation of children, especially young children, from their parents, and attention is drawn to the great variety of home backgrounds in relation to child rearing and training, as against the fact that the hospitals tend to impose a stereotyped set of standards, which must appear to be extremely confusing to the average child under five years of age. In the opinion of the committee it is essential that care of children in hospital should be based on mutual understanding of staff and parents, and that staff must take into account the fact that, with rising standards of living and education, a great many parents are aware of the elements of the emotional needs of infants and children, just as three decades ago parents were becoming well informed of the physical needs of their children.

The committee is in favour of the admission of mothers to hospital along with children under five years of age. In this respect it is of interest to note that James Robertson, the producer of the film "A Two-year-old Goes to Hospital",[3] has now, after waiting several years to find the right setting, produced a companion film "Going to Hospital with Mother".[4] This film was made at Amersham General Hospital, which, according to Dr. Dermod McCarthy,[5] had at the time when the film was screened been admitting mothers with children under five for three years, and they felt ready to have their work recorded although there was still much to be learned. This film shows the mother caring for her infant, engaging in conversation with other mothers and assisting in hospital chores, like making swabs. Apparently at this hospital mothers of seriously ill children are also admitted, and their anxiety does not appear to prevent them being good and efficient mothers under the careful tutelage of the staff. Where facilities do not exist for the admission of the mother with her child, the committee comes out strongly in favour of the wider use of home care and of the day hospital; where this is undesirable or impossible, daily visiting by parents or surrogates is recommended. Every aspect of hospital administration, as it affects the welfare of sick children, is considered by the committee, starting with preparation of the child for admission to hospital, reception and handling by all in the ward and at the places where tests and ancillary examinations are made.

This report, emanating from the British Ministry of Health, should do much to rekindle interest and stimulate further action in this perennial topic, not only in England but perhaps in Australia.

[1] Med. J. Aust., 1952, 1: 225 (February 16); 1954, 1: 563 (April 10); 1958, 2: 461 (October 4).

[2] "The Welfare of Children in Hospital", Report of the Committee, Central Health Services Council, Ministry of Health; 1959. London: Her Majesty's Stationery Office. Price: 2s. 6d. (English).

[3] A fully revised version of this film has just been issued.

[4] *Proc. roy. Soc. Med.*, 1958, 52: 381.

[5] *Ibid*: 583.

Abstracts from Medical Literature.

MEDICINE.

Respiratory Effects of Obesity.

R. M. Cherniack (*Canad. med. Ass. J.*, April 15, 1959) describes a train of effects occurring in obese persons resulting from the greater effort which fat people have to make in order to breathe. This is due to the greater resistance of the thorax to distension. Consequently the tidal air volume is less than it should be and there is a subtle tendency to hypoxia and hypercapnia. The hypoxia, despite compensatory erythrocytosis, leads to lassitude and headache; and the hypercapnia occasionally leads to acidosis, electroencephalographic changes and papilloedema.

The Indications for Surgery in Pulmonary Tuberculosis.

J. D. Steele (*Ann. intern. Med.*, January, 1959) discusses the indications for surgery in pulmonary tuberculosis. The use of antimicrobial agents has changed the role of surgery and also the choice of surgical procedures in this disease. The indications for surgery have become better established during the last five years as the potentialities and limitations of antimicrobial therapy have become better understood. Pulmonary resection is the most widely used surgical procedure and, in general, is indicated either when antimicrobial therapy has failed to close cavities, or in the case of fibrocaseous residuals when they are believed to be a likely cause of relapse. It is generally agreed that cavitary lesions, which have not closed after a reasonable trial with chemotherapy, should be resected when possible. However, the resection of stable, residual, fibrocaseous lesions is a more controversial subject. Surgical collapse therapy (standard or plombage thoracoplasty) may be preferable to resection in certain patients who are poor risks for resection, either because of loss of sensitivity of organisms to potent antimicrobial agents or because of considerable reduction in respiratory reserve due to extensive disease. Although the immediate results of most surgical procedures are well known, the evaluation of long-range results will have to await the results of further follow-up studies.

Acquired Aplastic Anæmia.

J. L. Scott, G. E. Cartwright and M. M. Wintrobe (*Medicine (Baltimore)*, May, 1959) analyse the cases of 39 patients with acquired aplastic anæmia, and review the pertinent literature. The condition is defined as a syndrome in which pancytopenia due to marrow destruction and inhibition is present and evidence of infiltrative disease of the marrow is absent. The disease affects all age groups and both sexes; purpura is the most frequent presenting symptom. Physical manifestations other than those of anæmia and thrombocytopenia are not striking. Distinct splenomegaly is most unusual. Bone marrow sections usually show reduced general cellularity, but variations ranging from total aplasia to apparent hyperplasia may be observed. Exposure to agents of probable ætiological significance was recognized in 12 of the 39 cases studied. Chloramphenicol, "Mesantoin", benzene, acetarsone and sulphonamides were amongst probable causative agents. Cortico-steroid therapy may occasionally be of benefit; two out of 24 patients receiving adequate steroid therapy in the present series improved significantly. The danger of serious infection during prolonged therapy should be recognized. The present status of splenectomy is discussed. Five out of 15 patients on whom operation was performed responded with a substantial reduction in transfusion requirements. The natural history of the disease is unpredictable. Partial or complete hæmatological recovery was observed in 14 of the 39 cases; the duration of the illness in these varied from three months to 10 years. Recovery was usually a gradual process even in cases in which splenectomy or steroid therapy was of apparent benefit. Twenty-one patients died of the complications of prolonged pancytopenia; hæmorrhage, particularly intracranial bleeding, was the most common principal cause of death.

Paget's Disease.

C. Bussolati and A. Doria (*Presse méd.*, February 14, 1959) have studied for several years six patients suffering from Paget's disease of bone, and have carried out new laboratory investigations. The results have led the authors to confirm the old theories of an inflammatory (bacterial or viral) origin for the disease. They state that critical assessment of hypotheses incriminating a metabolic disorder, hormonal influences and disturbed vitamin status favours the theory of inflammation as the source. The authors believe that future research should be aimed at identifying the ætiological agent.

Streptococcal and Non-Streptococcal Sore Throats.

V. Esmann (*Acta med. scand.*, volume 163, fascicule 4, 1959) studied 81 patients with sore throats, drawn from a number of general practices. In 42% this symptom was due to streptococcal infection. The author stresses that as streptococcal and non-streptococcal sore throats cannot be differentiated on the basis of clinical observation, routine culture of pharyngeal material for isolation of the appropriate organism is indicated. A marked increase in antistreptolysin titre was found to be a significant sign of streptococcal sore throat.

Beriberi Heart Disease.

R. H. Jones (*Circulation*, February, 1959) outlines the development of the current concept of beriberi heart disease, especially as seen in Western countries. The author emphasizes that some patients with known organic heart disease in congestive failure may have a coexisting factor of thiamine deficiency that will influence the clinical manifestation and necessitate supplementary vitamin B_1 therapy. For severe cases 100 mg. of thiamine by injection at eight-hourly intervals are advised. In the presence of œdema additional diuretics and sodium restriction are prescribed. The view that digitalis is of no value or that a good response to this drug denies the diagnosis of beriberi heart disease has been found to be untrue. Classical beriberi heart disease as originally described in the Orient was graphically portrayed as predominantly right-sided heart failure in the face of a hyperkinetic circulation. In Western countries many cases of beriberi heart disease do not conform to this dramatic syndrome. A broader diagnostic concept has permitted the recognition and treatment of an increasing number of patients who respond to thiamine after having been refractory to all other measures.

Mortality and Prognosis of Cardiac Infarction.

S. Helander and M. Levander (*Acta med. scand.*, volume 163, fascicule 4, 1959) have studied the primary mortality and the five-year prognosis of cardiac infarction. The primary mortality in their material, which is composed of 286 cases, was 32%. Group I, including patients showing the clinical picture of shock with marked fall in blood pressure, had a primary mortality of 54%; group II, patients manifesting no shock but otherwise presenting a fully developed clinical picture of cardiac infarction, with fever, raised sedimentation rate and leucocytosis, had a primary mortality rate of 27%; group III, milder cases with electrocardiographic evidence of infarction only, had a primary mortality rate of only 4%. Estimating the survival rate of those who survived the first attack of cardiac infarction, 58% were found to be alive after five years. Severity of initial infarction, as classified above, did not significantly influence the subsequent course. Comparison of these patients with a control group of the Stockholm population of the same age showed, however, a markedly increased mortality amongst cardiac infarction survivors. Amongst the electrocardiographic changes, evidence of atrio-ventricular and intraventricular heart block substantially worsened the prognosis.

Depressive Reactions in Hypertensive Patients.

R. M. Quetsch *et alii* (*Circulation*, March, 1959) set out to compare depressive reactions in hypertensive patients treated with rauwolfia drugs and those receiving no specific anti-hypertensive treatment. For this purpose they studied 387 patients seen at the Mayo Clinic during the years 1954 and 1955. It was found that of 202 patients that were treated with some preparation of *Rauwolfia serpentina*, 26% experienced a depressive reaction, and this was moderately severe or severe in 10%. In contrast, in a comparable control group of 185 hypertensive patients who received no anti-hypertensive medication, the authors found only 5% with depression. The evidence did not indicate any relationship of depression to the severity of hypertension, to drugs other than rauwolfia, or to the efficiency of treatment in lowering blood pressure. Depression occurred in more than half of those patients who had a history of depression prior to beginning treatment with rauwolfia and in almost a fourth of

patients without such a history. The dose of rauwolfia tolerated by different individuals varied, but no depressive reactions were observed in patients taking less than 0·2 mg. of reserpine daily. Although 60% of these reactions occurred within the first six months after treatment with rauwolfia was begun, several instances were observed where this reaction came on after one year of treatment. The authors conclude that patients taking *Rauwolfia serpentina*, whether as a whole root extract, alseroxylon fraction, or reserpine, require close observation indefinitely for any evidence of mental depression. They consider that in view of the frequency and severity of depressive reactions among hypertensive patients treated with rauwolfia, the physician must evaluate the indications for use of this drug with extreme care and whenever possible avoid its use altogether.

Atrial Septal Defect.

D. C. McGOON *et alii* (*Circulation*, February, 1959), from the Mayo Clinic, discuss 119 cases of atrial septal defect operated on at the Clinic between 1953 and 1958. The majority were operated on by an open technique utilizing the atrial well method. The total operative and post-operative mortality in this series was 12%. The authors found that five factors significantly raised the mortality rate, namely: (i) a history of clinical congestive heart failure; (ii) markedly elevated right atrial pressure; (iii) large right-to-left shunt; (iv) severely elevated pressure in the pulmonary artery; (v) markedly increased pulmonary vascular resistance. In ideally selected cases the operative and post-operative mortality for surgical closure of atrial septal defect was less than 2%.

Paget-Schroetter Syndrome.

J. T. PHELAN AND C. W. CRUMPTON (*Circulation*, March, 1959) report a case of so-called primary venous obstruction in the upper extremity, also known as the Paget-Schroetter syndrome, and review the literature pertaining to this subject. The condition represents an extravascular obstruction to the axillary or subclavian vein, with or without thrombosis, by adjacent bone and soft tissue structures. Clinically, the condition appears as a sudden non-œdematous swelling of one upper extremity with discoloration, pain and distended veins. Metastatic carcinoma involving the axilla, or direct pressure from a mediastinal or bronchial carcinoma, must be excluded in the differential diagnosis. Sometimes the condition appears to be related to some unusual muscular exertion. Treatment of this syndrome has been primarily conservative in nature; however, it would appear that early operative intervention with the purpose of removing an extravascular obstruction and reestablishing venous flow by surgical phlebotomy may be the procedure of choice.

Pulmonary Œdema.

W. F. MILLER AND B. J. SPROULE (*Dis. Chest*, May, 1959) give an account of the satisfactory treatment of acute pulmonary œdema with oxygen and a bronchodilator detergent aerosol with or without anti-foaming agents, administered by means of mechanically assisted intermittent inspiratory - positive - pressure breathing. The authors point out that the presence of viscid froth in the bronchial tree obstructs the distribution of the inspired oxygen, and they produce gas-exchange studies which show that in these circumstances pulmonary arterial blood traverses the lung through non-ventilated areas or perhaps through shunts. The improved ventilation effected by the treatment not only relieves hypoxia, which improves cardiac function and vascular tone, but increases lymphatic flow and speeds the reabsorption of the œdema fluid. The improved ventilation also relieves dyspnœa by decreasing the work of breathing.

Coronary Arteriography.

L. H. FRISCHE AND C. T. DOTTER (*Dis. Chest*, May, 1959) describe an improved method of determining the condition of the coronary arterial lumen with a view to the selection of patients for the surgical treatment of cardiac ischæmia. Under general anæsthesia a catheter is passed up the radial artery until its tip is seen fluoroscopically to lie in the first part of the aorta. A balloon near its tip is then inflated with nitrous oxide to occlude the aorta, and a volume of some 10 to 20 millilitres of a thorium dioxide suspension is injected into the aorta quickly under pressure. Serial radiography is initiated at the beginning of the injection and continued at the rate of one or two films per second for about six seconds. The balloon is deflated the moment the injection is complete. The catheter is then withdrawn and the artery repaired. The X-ray films show the coronary arteries very well; but the authors believe that even better results should be obtainable if the procedure were carried out during a period of induced cardiac arrest.

Simple Radiographic Aid in the Diagnosis of Pulmonary Embolism.

L. A. SOLOFF AND J. ZATUCHNI (*Amer. J. med. Sci.*, May, 1959) describe an early, hitherto unrecognized, simple radiographic aid in the diagnosis of major pulmonary embolism. The clinical history of an illustrative case is presented. The mid-right diameter of the cardiac silhouette is the greatest horizontal distance between the mid-spinal line and the right border of the cardiac silhouette in the frontal plane. This rarely exceeds 50 mm. in normal health. In 50 consecutive chest skiagrams of normal adults, 16 to 70 years of age, the mid-right diameter was 50 mm. or less in all but three. Conversely, a mid-right diameter greater than 50 mm. tends to be associated with an increased right atrial volume. Conditions other than right atrial enlargement which may increase the mid-right diameter are displacement of the cardiac silhouette to the right, chest deformities, cardiac tumours, diaphragmatic hernia, adjacent pulmonary or pleural disease, and pericardial disease. Therefore, the interpretation of the meaning of an increased mid-right diameter depends upon analysis of the circumstances under which such an increase occurs, and also upon exclusion of conditions other than enlargement of the right atrium. In the case reported, the mid-right diameter was normal in the chest radiogram taken on admission to hospital, but after pulmonary embolism had occurred this measurement was greatly increased; the right border of the cardiac silhouette also became more convex. Increase in the mid-right diameter with bulging of the right border of the cardiac silhouette was initially the only radiographic change. In cases in which the X-ray film of the lungs shows no abnormal signs, these changes in the cardiac silhouette may be very helpful, and may be the only radiographic evidence of major pulmonary embolism.

The Use of Chlorothiazide in the Nephrotic Syndrome.

J. E. BURCH AND H. A. WHITE (*A.M.A. Arch. intern. Med.*, March, 1959) present a study of 10 patients suffering from the nephrotic syndrome associated with various types of renal disease, who were treated with orally administered chlorothiazide. The drug was found to be a successful and sometimes dramatic diuretic agent. When properly integrated with corticotrophin or corticosteroids, bed rest and other well-established clinical procedures, it should prove to be therapeutically beneficial in patients with the nephrotic syndrome, and should at least be given therapeutic trial. Whether or not it has any "curative" value remains to be determined, but it may prove valuable indirectly by reducing arterial blood pressure and eliminating the waterlogged environment of vital cells of the body, including those of the nephron.

Benign Hypertension.

A. A. POLLACK AND J. R. GUDGER (*A.M.A. Arch. intern. Med.*, May, 1959) discuss benign hypertension based upon a survey of 2500 life insurance policy files. It is concluded from among a highly selected group of persons with mild or moderate arterial hypertension, but otherwise in good health, that there is no evidence that lability of the blood pressure is a significant factor in the moderately increased mortality experienced. Thus, the observed fluctuations in blood pressure in this series did not indicate that the life span in these persons would be greater than that of persons with constantly observed hypertension. Therefore, it would seem proper to include a proportionate number of elevated readings with normal ones, in the determination of the average blood pressure for an individual person. The data obtained support the generally accepted conclusion that the significance of hypertension becomes less important as the age of the person advances. The results also suggest the desirability for early recognition of temporary elevations in blood pressure, and their importance to otherwise healthy persons.

The Polystethoscope.

A. BRISKIER (*Presse méd.*, March 28, 1959) describes a stethoscope, which he calls the polystethoscope, with four chest pieces, each corresponding to a particular region—mitral, pulmonary, aortic or tricuspid—on the thoracic cage. It is possible with this instrument to listen to all the sounds from all the cardiac foci, and to eliminate any one of them or select those requiring further study. The instrument is easy to use, light and practical.

Brush Up Your Medicine.

OTITIS EXTERNA.

The main objects of this paper are (i) to discuss the various ætiological agents responsible for otitis externa, and (ii) to indicate the treatment necessary for each particular type.

Ætiology.

An important factor in the initiation of an attack of otitis externa is interruption of the continuity of the epithelial lining of the external auditory canal. Under tropical conditions, the sequence of events is probably as follows. Initially, persistent high temperatures and humidity, or repeated wettings by swimming and taking showers, cause œdema of the top layers of the skin. This results in occlusion of the ducts of the apocrine and sebaceous glands, with the loss of the normal oily protective coating on the skin, which becomes dry, itchy and scaly. Scratching of the unhealthy lining readily breaks it down and allows introduction of infective agents. In subtropical zones, the most important underlying cause of infection is probably unhealthiness of the lining resulting from so-called seborrhœa. Some authorities report that there is a change in the skin pH from the normal acid to an alkaline state.

Otitis externa occurs equally in both sexes and at any age. It is not infrequently seen in early infancy, resulting from secondary infection of retained vernix caseosa and epithelial debris. Also, for reasons that have been mentioned, it is seen most commonly in the tropics. As many will recall, it was one of the chief causes of morbidity in service personnel in northern Australia and in New Guinea.

The various ætiological agents concerned in external otitis may be listed as follows:

1. Furuncular infection, due to staphylococci.

2. Fungal infection, including infection with *Aspergillus niger* and moniliasis. The latter is commoner now than formerly, owing to the increased use of antibiotics. This group accounts for 15% to 20% of cases.

3. Seborrhœa and psoriasis.

4. Infection with Gram-negative organisms, especially *Proteus* and *Pseudomonas pyocyanea*. This is the commonest single group. Some of these infections are primary, but many are probably secondary to mild unrecognized seborrhœa.

5. Allergy. This includes not only ordinary eczema, but also reactions due to locally applied substances, such as sulphonamide drugs, penicillin and other antibiotics. In this regard, allergic otitis externa occurs most frequently when the substances are used in a pure form, such as powder. It does not seem to be common with the 1% to 10% ointments and solutions.

6. Unsuspected foreign bodies. A lost piece of cotton-wool is especially common.

Acute Otitis Externa.

Symptoms.

In acute otitis externa pain is always present, and is often very severe. Strangely enough, in some fungal infections pain is a prominent feature, even though there does not appear to be much local reaction in the ear. Pain on chewing is a characteristic symptom. Discharge is not present in the early stages of a furuncle, but is usually found in other types of acute otitis externa. The degree of deafness is important. When deafness is only slight or absent, the condition is usually external otitis, though if the canal is filled with debris deafness will be severe, whatever the condition of the middle ear.

Signs.

The signs depend mainly on the type of infection. Tragal tenderness is invariably present. When this is elicited, it is indicative of external otitis. Similarly, pressing on the cartilaginous meatus from below or pulling back the pinna will cause pain. The appearance of the canal is important. Some degree of swelling is always present. This may be localized, as in the case of a furuncle, or generalized, as is more usual. In fungal infections, the presence of moist blotting-paper masses is characteristic. In addition, black spores, indicating *A. niger*, may be noted.

The drum itself varies in appearance. Often this is perfectly normal; but if the drum is involved in the process, it may become hyperæmic, and thereby suggest the presence of a middle-ear infection. The details usually remain discernible. The differential diagnosis is at times not easy.

The discharge is usually thin and watery; it may be clear or purulent, according to the type of condition. It is never thick, mucoid or sticky as in Eustachian tube infections.

In severe external otitis, the spread of infection can produce a picture resembling mastoiditis. In these cases pyrexia may be present, with pre-auricular and post-auricular swelling, the pinna being displaced forwards. The swelling is due either to enlargement of regional pre-auricular and post-auricular glands, or to spreading cellulitis. In either condition suppuration may occur.

Differential Diagnosis.

The following points assist in the differentiation of acute external otitis from mastoiditis:

1. A mastoid infection is usually preceded by an upper respiratory tract infection with associated nasal and pulmonary signs.

2. Mastoiditis never causes tragal tenderness or pain on chewing.

3. A normal drum suggests external otitis; an inflamed drum can be due to either otitis media or otitis externa.

4. The canal in mastoiditis is usually normal in appearance, though in some cases there is a localized postero-superior sag. Pus in the mastoid can discharge into the external meatus through a fistula in the postero-superior wall. In such cases the condition resembles a furuncle.

5. In mastoiditis the hearing is usually moderately diminished; however, it may, rarely, be almost normal.

6. Thick, mucoid discharge denotes middle-ear infection. A pulsating discharge through a perforation in the drum is pathognomonic of otitis media. The use of a Siegle's speculum to detect a small perforation is often of assistance in distinguishing a middle-ear infection from a purely external condition.

7. The swelling in mastoiditis is never anterior and is usually posterior; it may be above the ear if the zygomatic cells are involved. In Bezold's abscess, the swelling is in the upper end of the cervical chain, below the ear. The swelling is usually fluctuant.

8. In difficult cases an X-ray examination may help to determine whether the mastoid process has been involved.

Chronic Otitis Externa.

Symptoms.

In chronic otitis externa there is persistent or recurrent itching. A complaint of itchiness and irritation in the ear always suggests underlying external otitis. In certain psychoneurotic patients, itching may be the only symptom; close questioning will often reveal the presence of irritation of other orifices, such as pruritus ani.

The discharge, as an acute external otitis, is usually thin and watery, especially in the eczematous type of case. When it is profuse, the discharge may produce secondary dermatitis down the neck and on the side of the face.

In severe cases some pain and tenderness may be present; these are not invariably found in the chronic condition.

As in acute external otitis, deafness is only slight once the canal has been cleared of any debris.

Signs.

The canal varies in appearance. In seborrhœa without infection, it may be simply dry and scaly. The lesion is limited to the meatal entrance and the adjacent external area. Usually dandruff and scaly blepharitis are also present. When infection, whether primary or secondary, is present, the walls of the meatus may be swollen, red, weeping and excoriated. In the exudative phase, eczema presents an appearance similar to that found in the infected group, but the presence of lesions elsewhere suggests the condition. In the chronic scaly stage, eczema resembles so-called seborrhœa. The degree of swelling varies. In some cases of *Proteus* infection, the discharge may have a characteristic greenish appearance.

The drum may or may not be engorged and red; often its appearance is normal.

The hearing is usually good.

Inspection of the scalp often reveals seborrhœa, or there may be patches of eczema, psoriasis or fungoid infection elsewhere on the body. Blepharitis may be found on examination of the eyelids. One should always question the patient about the occurrence of past or present skin lesions.

Investigation of patients suffering from external otitis should include the taking of an aural swabbing for culture and sensitivity tests, and microscopic examination of the debris, to exclude the presence of a fungal infection. In exceptional cases an X-ray examination of the mastoid process will help to differentiate between external otitis and mastoiditis. When eczema is present, skin tests are sometimes useful.

Differential Diagnosis.

In the differential diagnosis, there are two well-known conditions which produce changes in the external auditory meatus, but which are primarily due to infection at another site. These are bullous hæmorrhagic otitis and herpes zoster oticus.

Bullous hæmorrhagic otitis commonly presents as hæmorrhagic bullæ on the ear drum itself (so-called myringitis), but can also occur as discrete lesions along the canal wall. It is usually secondary to a streptococcal throat infection. It is painful during the formative stage. It will rapidly respond to treatment with antibiotics and sulphonamide drugs.

Herpes zoster oticus (Ramsay Hunt syndrome) may occur as a simple herpetic eruption with pain and no neurological signs; but usually there is a facial nerve lesion, and sometimes an eighth nerve lesion, with or without labyrinthine symptoms. Eruption is preceded by preherpetic pain localized to the ear and mastoid process. This is followed by an herpetic eruption on the tympanic membrane, in the external auditory canal, on the concha, the antitragus and the antihelix and its fossa, and occasionally on the mesial surface of the auricle and over the mastoid process.

Treatment.

It has been the experience of most otologists that systemic chemotherapy is being used far too frequently for a condition that essentially requires local treatment for its cure. In one case that comes to mind, a woman had received over 250 capsules of antibiotic agents for a fungal infection, needless to say, without benefit. The condition rapidly responded to adequate local measures.

The treatment depends on the ætiology. It cannot be too much emphasized that one must not rush into the systemic administration of antibiotics. Local treatment is all-important, and without this any systemic treatment will be ineffective. The main principles of treatment are as follows.

1. Except in the case of uninfected dermatoses and furuncles without debris, thorough cleansing of the auditory canal is essential.

2. Local causative agents should be eliminated by appropriate medication. Certain American opinions suggest that medicaments for local application should be acid in nature, the acetate radical being especially effective. However, this would not appear to be very important, since specific antibiotics are now so effective.

3. Systemic therapy is required when infecion is spreading into the deeper tissues.

4. Pain and sleeplessness must be relieved.

5. The external auditory canal must be restored to a normal physiological state.

Treatment will now be considered according to the ætiology of the condition.

Furuncle.—The treatment here is to pack the ear tightly with a specific anti-staphylococcal ointment, such as "Aureomycin" (3%), or "Terramycin" ointment in combination with polymyxin. The old standby, ichthyol and glycerine, still has its use, although it is not nearly so effective as the modern antibiotic agents. Ideally one should attempt a culture of material from the ear, in order to determine the antibiotic to which the staphylococcus is sensitive; but this is not always possible under practice conditions. As is well known, the staphylococcus is rapidly developing resistance to penicillin; figures show that 70% to 80% of these organisms are now resistant to this agent. However, the staphylococcus responds well to "Aureomycin", "Terramycin" and "Chloromycetin", and therefore it is wise to use one of these agents initially. These substances should be given parenterally if the furuncle spreads as a cellulitic condition, or if secondary glandular involvement occurs. Heat is very comforting and important in this condition. It is administered in a dry form—for example, with an infra-red lamp, short-wave diathermy apparatus or hot-water bag. Anodynes are usually essential, as the condition is often very painful. Incision of a furuncle can be carried out occasionally, but one runs a danger of perichondritis if the perichondrium is damaged. For this reason the procedure is not regarded favourably by many otologists. In recurrent staphylococcal infections, one should always test the urine to exclude the possibility of diabetes mellitus. I have found that a course of staphylococcal vaccine injections or an autogenous vaccine is very valuable in these cases. X-ray therapy is used by some otologists to prevent recurrences. I have had no experience with this method.

Gram-Negative Infections.—Here the culture will determine which organism is present, and sensitivity tests will show which antibiotic ointment to apply. Usually "Aureomycin" ointment, "Terramycin" ointment with polymyxin, or "Chlormycetin" drops will prove successful. I no longer find it necessary to use acetic acid, which probably depended on acidification for its effectiveness. There is, of course, a danger that sensitivity may develop in these cases, and one should always be on the lookout for this occurrence. Neomycin ointment is used by many otologists, as it is considered less likely to produce such reactions. Sensitization is apparently much more prevalent with pure powders than with the weaker ointments and drops.

In severe infections the parenteral administration of antibiotics may be necessary, and streptomycin injections will often be useful here. Again, the application of heat is very helpful in these cases.

Fungal Infections.—I never use antibiotics, either parenterally or locally, in these infections. In my experience, the condition appears to be aggravated by them. The cure depends on (a) thorough cleansing of the ear, which should be syringed daily until the condition is brought under control, and (b) the use of various fungicidal agents. Methyl alcohol (pure) is an agent often used in the laboratory to inhibit the growth of fungous infection on culture plates, and clinically it has also proved useful. It may be necessary to dilute it, as initially it can cause smarting. Half-strength "Mycozol" solution is also a useful application. Subchloride of mercury (1: 2000) in spirit has been used frequently. More recently "Mycostatin" ointment has proved useful. After the condition has subsided, the ears should be watched for some weeks, otherwise relapses may occur from odd spores left behind.

Monilial Infections.—The ears should be thoroughly syringed out, and then 1% to 2% gentian violet solution applied three times per day.

Seborrhœa.—In these cases it has long been the custom to treat the scalp. This involves frequent shampooing with such agents as sulphur soap, and the regular application of medicaments, such as sulphur and salicylic acid ointment. The ear responds well to local treatment with hydrocortisone ointment, usually combined with some antibiotic. The ointment is applied twice or three times a day, especially at night. Irritation is often an annoying feature in these cases, and the continual scratching of the ear by the patient only helps to aggravate the condition. In order to overcome this, hydrocortisone ointment is useful. The exhibition of phenobarbital is also helpful from this point of view. The old standby, sulphur and salicylic acid ointment, still has its uses in these cases. Silver nitrate solution (20%) may be of help in chronic cases in which secondary infection has occurred. It should be painted on daily.

Allergic Conditions.—These are often low-grade, but of great chronicity. Phenobarbital and antihistamines can be used to allay the irritation which is so common a feature, and the former can also be given for psychoneurotic factors, which play a large part in eczema. The local treatment includes such agents as gentian violet, Burow's solution, "Vioform" cream and sulphur and salicylic acid ointment. Once again, a very useful solution is silver nitrate (20%). We all have our own favourite applications for use in these cases. In many cases, the condition will not respond to these medicaments. However, hydrocortisone ointment proves very helpful in many of these resistant eczematous conditions. It can be used as 1% to 3% ointment applied three times daily. In very severe cases, cortisone may be given by mouth. Ointments combining hydrocortisone and antibiotics are now available. In certain cases when the condition is resistant to other methods of treatment, X-ray therapy to the ear can be tried. However, beware of the danger to the ceruminous glands from excessive dosage. Where definite sensitizing agents

are present, as determined by skin tests, a course of desensitization can be given. However, in my experience, it has not proved of any particular value in these cases. Septic foci should be eliminated on general grounds. It is still debatable whether their removal acts specifically on the allergic lesions. When the eczematous condition extends down the skin of the neck, the usual preparations advised for dermatitis are indicated, such as calomine lotion with pine tar, zinc cream, Hutchinson's lotion, etc.

Conclusion.

In conclusion, there are several important points in the management of all types of external otitis.

1. Advise the patients to keep the ears dry. They should not swim, and should take great care when taking showers or washing their hair.

2. Dry cotton-wool must never be used as a plug; it should always be well covered with some lubricant, lanoline or "Vaseline"; otherwise, when the discharge dries, the wool adheres to the skin, and the latter is needlessly damaged as the wool is removed.

CLIVE PYMAN, F.R.A.C.S., D.L.O.
Melbourne.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on March 18, 1958. DR. NORMAN ROSE, the Medical Superintendent, was in the chair. The principal speaker was DR. R. G. LEWIS.

Clinical History.

A widow, aged 62 years, had been treated for three years for mild symptoms—headache, dizziness, exertional dyspnœa and palpitations—associated with hypertension, with a systolic pressure of up to 240 mm. of mercury. Four days before her admission to hospital she felt suddenly "queer" while shopping, made her way to an hotel, complaining of crushing retrosternal pain, giddiness and blurred vision, and had a brandy. She was soon overcome with a drenching sweat, vomited and lost consciousness. She recovered enough 15 minutes later to make her way home, where she had a bout of diarrhœa and marked paræsthesiæ in both arms. After she had been in bed a few hours she complained of severe lumbar backache, cramps in the right leg, and a different pain across the front of the chest. Her local doctor found her pulse regular at a rate of 94 per minute and her blood pressure to be 240/140 mm. of mercury. He gave her an injection of morphine, which relieved her backache; but the chest pain persisted. Next day she still had slight retrosternal pain and also pain in the right upper quadrant of the chest, worse on breathing deeply. The blood pressure was 180/120 mm. of mercury and her temperature was 99·6° F. When examined by a consultant on the third day, she appeared to be in no distress, had no pain and moved freely in and out of bed. The recorded fidings were: a blood pressure of 140/100 mm. of mercury in the right arm and 100/80 mm. in the left; minimal clinical cardiac enlargement; no evidence of congestive heart failure; palpable carotid pulses; no thrills, but a rough, harsh, systolic murmur heard best at the base.

On her admission to hospital, she said she had not been entirely free of chest pain since the onset of the illness, and at times there had been a feeling of constriction. However, at the time of her admission it had almost passed off, though she still had a slight aching pain in the back. Nausea and flatulence had been present since the onset of the illness, and she had not eaten. Specific interrogation revealed that she had not previously had pains in the chest, ankle swelling, nocturnal dyspnœa or loss of weight. She had had polyuria, urgency of micturition, nocturia and pruritus vulvæ, but no other symptoms referable to the genito-urinary system. She had had blurred vision on and off for the past few months and tinnitus for years, and her memory and concentration had been poor lately. In addition, she had had drenching nocturnal sweating and pains in many joints, and had been told she had polyarthritis. Her past history included mumps, measles, typhoid fever and pneumonia before she was eight years old, and a miscarriage and septicæmia at 22 years of age. She smoked a few cigarettes each day and had a fairly heavy, constant alcohol intake. Her mother had died in childbirth at an early age.

Examination showed the patient to be an elderly, plump, plethoric woman, in no obvious distress. There was no fever. Her hands and feet were said to show arthritic changes, but movement was painless and not limited. Her pulse was regular, the rate being 100 per minute, and the vessel wall was not palpable. The left radial pulse was diminished in amplitude. The jugular venous pressure was not raised, though the veins of the upper limb were distended. The blood pressure in the right arm was 140/90 mm. of mercury and in the left 100/30 mm. The apex beat was five inches from the midline in the fifth intercostal space. A harsh systolic murmur was heard best at the apex and in the aortic area, but was also heard along the left side of the sternum, in the neck and in the axilla. There was tenderness in the lumbar regions. The ankle jerks were absent and the knee jerks diminished. No other abnormalities were noted and the urine was normal on full examination.

Fifteen hours after her admission to hospital the patient suddenly became unconscious and cyanosed, with stertorous respiration, and died.

Clinical Discussion.

DR. N. ROSE: On reading this case it seems particularly straightforward—in fact, so straightforward it is frightening. Our speaker today is one of the recent acquisitions to the honorary medical staff, Dr. R. G. Lewis, and I now call on him to discuss this case.

DR. R. G. LEWIS: Dr. Rose, Ladies and Gentlemen. Firstly I would like just briefly to run through the story as we have it. Today we are disussing the diagnosis in a widow of 62 years, whose final illness lasted five days from onset to death. To begin with, I would like to take the final illness first. Four days before admission to hospital she felt suddenly "queer" whilst shopping, made her way to an hotel, complaining of crushing retrosternal pain, giddiness and blurred vision, and had a brandy. She was soon overcome with a drenching sweat, vomited and lost consciousness. She had recovered enough 15 minutes later to make her way home, where she had a bout of diarrhœa and marked paræsthesiæ in both arms. After she had been in bed a few hours she complained of severe lumbar backache, cramps in the right leg and a different type of pain across the front of the chest. We are not given any details as to just what this different pain was; however, evidently it was still precordial, although of a different quality. The local doctor found a regular pulse and a raised systolic and diastolic blood pressure, and he gave her an injection of morphine which relieved the backache, but the chest pain persisted. So, in the first day of the illness, the important things were that she had a crushing pain in the chest which was retrosternal, she lost consciousness and she sweated profusely, that she had some paræsthesiæ in both arms and severe lumbar backache, and that morphine did not relieve her chest pain completely. I think that these are important facts.

Then, the next day, she still had slight pain retrosternally, and also in the right upper chest worse on breathing deeply. That is the first time that the latter pain had been mentioned. Her blood pressure was still elevated—perhaps not quite so high as before—and she had a temperature of 99° F.

On the third day, when she was seen by a consultant, she appeared to be in no distress, had no pain, and at this stage it was found that her blood pressure was 140/100 mm. of mercury in the right arm, and 100/80 mm. of mercury in the left arm. So this is the first stage at which there has been any fall in blood pressure, and that was on the third day. Also a rough, harsh, systolic murmur was heard, and we are given a little more detail regarding that murmur when she was admitted to hospital.

On admission to hospital, she claimed then that she had not been entirely free of pain, although the day before she evidently had no pain for some while, and she also stated that there had been a feeling of constriction. However, at the time of admission, the chest pain had almost passed off, but she still had an aching pain in the back which I take to be in the lumbar region, just as the previous pain was.

With regard to specific interrogation, we learn that she had no angina of effort in the past, nor any symptoms related to ankle swelling, nocturnal dyspnœa or weight

loss. However she had—and we are not told for how long—complained of polyuria, urgency, nocturia and pruritus vulvæ. She had blurred vision on and off for a few months, tinnitus for years, and her memory and concentration had been poor of late. In addition, she had drenching nocturnal sweating. The length of that symptom would be important, but we are not told that. Also she had had pains in many joints, and had been told she had polyarthritis. As well, for three years, she had headache, dizziness, exertional dyspnœa and palpitations, and had a systolic hypertension at least. The only other possibly relevant fact is that she had a heavy constant alcohol intake.

Now, on examination, we are told she was elderly, plump, plethoric and apyrexial. Her hands and feet were said to show arthritic changes, but movement was painless. I am not going to say much more about these changes. I wondered whether perhaps she had some Heberden's nodes, but we are not told any more about these joint changes. She had a regular pulse, and the important thing is that the left radial pulse was diminished in amplitude, and the difference in the two blood pressures in each arm is quite significant. It was 140/90 mm. of mercury in the right arm and 100/30 mm. of mercury in the left arm. The apex beat was five inches from the mid-line—in other words she had some cardiac enlargement—and a harsh systolic murmur was heard best at the apex and the aortic area, also along the left side of the sternum, in the neck and in the axilla. I think at this stage we can say that this murmur was probably an aortic murmur being heard in the neck. The fact that it was heard in other areas does not matter a great deal, and I propose to assume that the murmur came from the aortic area. She was also tender in the lumbar regions. The ankle jerks were absent and knee jerks diminished, which may have been related to her previous alcohol intake. There was no mention of calf tenderness, however, and she was an obese elderly woman, and the diminution in the reflexes I think is quite consistent with these facts. The urine was clear, and there was no other abnormality mentioned. In other words, I take it that her fundi showed no abnormality.

Now I wonder if we can get any help at all from the past history. The things in the past history that I would like to discuss at this stage are polyuria, urgency, nocturia and pruritus vulvæ. She was an obese woman, and I would like to postulate at this stage that she quite possibly had diabetes. I do not think that is the important condition from which she suffered, but I think she possibly had diabetes with perhaps some bladder infection, in view of the urgency. The fact that she had no glycosuria in one specimen I do not think is important.

At this stage I think it would be appropriate to discuss the causes of acute chest pain—relevant of course, to this patient. I do not wish to go into all the causes of chest pain, but I want to discuss it more from the point of view of pain in the chest which is severe, and which causes death.

I think there are three groups which we should discuss: pain which is pulmonary in origin, pain which is related to the heart and great vessels and pain which is related to other viscera. To start with, we will discuss chest pain which is related to the lungs and pulmonary system. First of all, pleurisy, empyema and pneumonia can cause acute chest pain. In this case there was no pyrexia. An acute chest infection can occur without any pyrexia, but in that case the patient is usually quite shocked, and also in this case there were no physical signs, so I think we can exclude this cause. Spontaneous pneumothorax should be considered in anyone with acute chest pain; but in this patient no signs in the chest were found and so I do not think we need discuss that any further. Carcinoma of the lung should be considered—not that I think an uncomplicated carcinoma could have caused this story, but the possibility of a carcinoma perhaps infiltrating the œsophagus causing perforation and mediastinitis should be borne in mind.

With regard to chest pain due to other viscera, the things which should be discussed are first of all spontaneous rupture of the œsophagus. I have seen quite acute chest pain occur in spontaneous rupture of the œsophagus. It is quite commonly not diagnosed until autopsy, and it is commonly due to a bout of vomiting following a heavy meal or alcohol. The vomiting is followed by pain, shortness of breath, cyanosis and shock. Rupture could be associated with a carcinoma or foreign body of the œsophagus. For the reason that this patient did not have a bout of vomiting first and there were no signs of effusion or subcutaneous emphysema found, I think we need not discuss spontaneous rupture of the œsophagus any further.

This pain was typically chest pain; but high intra-abdominal conditions should be considered at the same time, such as a high peptic ulcer which has perforated or a subphrenic abscess. But in these conditions, although there may be chest pain, I think there should be some abdominal pain too, and I do not propose to discuss them any further.

So now we come to diseases of the heart and great vessels, and I feel that it is in this group that the patient's illness lies. First of all, I would like to discuss pulmonary embolism. This patient was an obese lady, and although she had no preceding period of bed rest, this is not necessary to cause a femoral vein thrombosis which may give rise to emboli. She did have some cramps in the calf, but that did not occur until after the acute attack. She had no rise in jugular venous pressure, but there is mention of the veins of the upper limb being distended. It does not say which upper limb, nor does it say both upper limbs. I admit it is difficult to see distended veins in an obese person; but the significance of these distended veins in the upper limb I find difficult to explain. I do not think there is any suggestion of mediastinal obstruction, and these veins in the upper limb may have been associated with raised venous pressure which was not visible in the neck. The pain did go to the right upper chest, and it was worse on deep breathing, which is a point in favour of pulmonary infarction. However, no hæmoptysis occurred, and we are given a lot of other symptoms to explain, which we cannot explain by virtue of pulmonary embolism.

The second disease I would like to mention is rupture of an aneurysm of the aorta, and by this I mean a saccular or fusiform aneurysm. This patient's story from onset to death is far too long, I think, for rupture of an aneurysm of the aorta.

Pericarditis can occur with chest pain, as was present in this case. As she had a lot of drenching nocturnal sweats, it makes one wonder whether she had tuberculosis and tuberculous pericarditis. However, tuberculous pericarditis commonly occurs in a younger age group than this. No friction rub was heard, which of course does not exclude it; but once again we have other symptoms to explain which cannot be explained on the basis of pericarditis alone.

And now bacterial endocarditis. Acute chest pain in bacterial endocarditis is quite unusual—that is, assuming that the valve involved for the reasons I have stated before was the aortic valve, from which an embolus would not go into the lung, but would go peripherally. She also had no diastolic murmur which I think would be very unusual in an endocarditis of the aortic valve. Perhaps an embolus could break off and obstruct the coronary artery, thereby causing acute chest pain. However, once again there are other things which I cannot explain on the basis of this diagnosis, but I will mention that again later when I discuss one other condition.

Now I come to the two conditions which must be discussed most fully, and two which are the most important in the differential diagnosis of this patient. These are myocardial infarction and dissecting aneurysm of the aorta.

First of all, in myocardial infarction pain in the back can occur, but is uncommon. Moreover, we were told that this was lumbar back pain, and I think that is a little low for myocardial infarction. Secondly, the patient's chest pain persisted for rather a long time, although when she was seen on the third day she said that she had no chest pain. On admission to hospital she said she had not been completely free of chest pain, and pain going on for five days in myocardial infarction and not relieved by morphine is rather unusual. Of course the pain spread to the arms, which is consistent; but she did have unequal pulses, and that is an important fact which I would like to discuss with the remaining condition—dissecting aneurysm.

Dissecting aneurysm is admittedly more common in men. It is quite common in this age group, and 75% of cases are over 40 years of age. She was hypertensive, and the vast majority of patients who develop a dissecting aneurysm over the age of 40 are hypertensive. The pain was very severe, and it was not relieved by morphine, which again is consistent. She lost consciousness, which would fit in with either of the two conditions, myocardial infarction or dissecting aneurysm. She was giddy. She had no aortic diastolic murmur; which I think would make

dissecting aneurysm completely diagnostic in this case; however, the fact that it is not present does not exclude the diagnosis. She also had no neurological signs, which once again do not always occur; but she did have some lumbar backache, which is quite common in a dissection of the aorta. And the most important thing is that she had paræsthesiæ which spread to the arms, and she had unequal pulses in the arms—the left being of less amplitude than the right. She was quite hypertensive at the start, and the blood pressure remained up for the first two days of her illness, which is unusual in myocardial infarction, in which the blood pressure usually drops reasonably quickly.

Now, can we obtain any help from the past history? She was hypertensive, and this does not help us one way or the other to differentiate between those two last-mentioned conditions. The hypertension was evidently not malignant—she had no abnormality in the urine, and there were no fundal changes. She had drenching nocturnal sweats, and that is the symptom which I think may be very important, but I cannot quite say why except that I will make a suggestion later. In anyone who is hypertensive and who sweats, one should consider phæochromocytoma. However, there were only nocturnal sweats, and there was no story of the acute hypertensive eposides of phæochromocytoma. Again, drenching nocturnal sweats bring to mind bacterial endocarditis.

Another point in the past history is the presence of pains in her joints. Did she have an arteritis, such as polyarteritis nodosa, which caused her joint troubles—polyarteritis nodosa which involved the coronary arteries and caused myocardial infarction? Polyarteritis nodosa usually occurs in a younger age group than this, but not invariably. What of these associated features that she had? She had hypertension, she was obese, I postulate that she possibly had diabetes, and of course that is the type of female patient in whom myocardial infarction does occur. But once again these things are all consistent with dissecting aneurysm, and again, which I did not mention before, of course dissecting aneurysm can involve the coronary artery and cause myocardial infarction.

Now I would just briefly like to mention what help we could possibly get from investigation. This case is presented purely as a clinical case, and all we have are the history and physical findings. I will mention five investigations which may have helped us. (i) A full blood count—a leucocytosis could be present in either dissecting aneurysm or myocardial infarction. (ii) The erythrocyte sedimentation rate can be raised in either condition. However, it is interesting that it can be raised up to 100 mm. per hour in dissecting aneurysm, and it might take four to eight weeks to return to normal. (iii) A chest X-ray—left ventricular hypertrophy can occur in either condition—she was hypertensive; but if we have an earlier X-ray to compare, a recent X-ray may show widening of the aortic shadow as a result of dissecting aneurysm. Another radiological sign, which I have never seen, is widening of the distance between calcium deposition in a plaque of atheroma—seen also in a previous X-ray—and the aortic wall, and this is diagnostic of dissecting aneurysm. (iv) Of what help could the electrocardiogram be? Signs of left ventricular hypertrophy could be present in either condition. In dissecting aneurysm *S-T* segment elevation and *T* wave inversion may be seen, but *Q* waves are unusual unless, of course, the dissection has involved the coronary artery. Heart block, fibrillation or the changes of pericarditis may occur in either condition. (v) Serum transaminase is a recently described investigation, which is of value in differentiating myocardial infarction from dissecting aneurysm, provided of course that the dissection does not involve one of the coronary arteries and cause infarction itself. Elevation of the serum glutamic oxalacetic transaminase (S.G.O.T.) is the one of particular value in myocardial infarction. The level rises approximately six hours after the onset of pain, and steadily rises to a peak within 48 hours and falls to normal over the subsequent three to six days. The level may not reach a very great height, but serial readings showing a rise and a subsequent fall are regarded as significant. In acute coronary insufficiency without infarction, the level of S.G.O.T. is not raised. The titre does not rise until there is actual myocardial necrosis with liberation of the enzyme from the damaged cells into the circulation. It is important to realize that this test gives a positive result in the first 48 hours, before the white cell count and sedimentation rate alter. From reports, it is more reliable than the two latter tests, which may show no abnormality in myocardial infarction. The level of S.G.O.T. may also be raised in hepatocellular injury, such as viral hepatitis and malignant deposits in the liver. However, in liver disease the serum glutamic pyruvic transaminase (S.G.P.T.) is also raised. In myocardial infarction, the level of S.G.P.T. is not significantly raised.

So what is my final diagnosis? It is dissecting aneurysm of the aorta, the cause of it being uncertain. It may be due to cystic medionecrosis, which commonly occurs. There is no suggestion of Marfan's syndrome in this case, in which dissecting aneurysm may occur and which is usually in a younger person. There is no mention of any high arched palate, lens dislocation, pes excavatum or any other congenital abnormality. Giant cell aortitis, which also occurs in association with a dissecting aneurysm, is usually in a younger age group. Could it be due to bacterial endocarditis involving the aorta and the dissection arising there? This must be very unusual, should it occur, and I certainly have never seen it. I mention this on account of the drenching sweats, which I am unable to explain except on this basis. With regard to the mode of death, 15 hours after admission she suddenly became unconscious and cyanosed with stertorous respiration, and died. Those findings are quite consistent with a rupture into the pericardium, which is by far the most common mode of death in dissecting aneurysm of the aorta. As well, as I mentioned previously, I wonder if this patient had diabetes.

Dr. Rose: Dr. Lewis's arguments I am quite certain will lead to dissecting aneurysm being a very short-priced favourite in this field. I just wonder whether it is the right answer, and I would like to hear from the physicians or surgeons in the audience who do not know the diagnosis.

Dr. K. B. Noad: I must say that for once I thought the protocol reasonably straightforward, and I reached the same conclusion as did Dr. Lewis—dissecting aneurysm. I find the same difficulties in finding a cause for the drenching sweats. The drenching sweat at the time of onset is of course easy to explain, and it is a common accompaniment of cardio-vascular disasters; but whether the sweats could have been associated with the arthropathy I do not know. She was told she had polyarthritis; yet on examination there was no evidence at least of a rheumatoid form of arthritis, so I too have doubt as to the cause of those sweats. Perhaps she had too many bedclothes on, which can be a cause of severe sweats. I, too, think she had a dissecting aneurysm of the aorta; there is some evidence in the protocol in favour of that, as Dr. Lewis pointed out, and I find that conclusion hard to escape.

Dr. David Failes: I must agree with Dr. Lewis in the diagnosis of dissecting aneurysm. I think the different blood pressure in the arms, which was apparently observed on more than one occasion, seems very definite and hard to explain on any other basis. I agree with the diagnosis here.

Dr. B. M. Hurt: I feel that it is not so much a problem of diagnosis in this case as some of the associated things that come to mind. After all, we have here a classical history of a vascular disturbance, and I have no doubt this woman had a dissecting aneurysm. The site of her pain was retrosternal, its quality was crushing and vice-like, it radiated to the back, its duration was longer than a quarter of an hour, and it was associated in some respect with exertion. We are at liberty to call this myocardial infarction; but we must go further in view of the radiation of the pain and the various organs that have been affected. One of her pains was low in the abdomen, she had pain in the loin, she had tender kidneys, and I believe that we have to say this dissection extended down the aorta and involved her iliac vessels, because one of her legs had a cramp in it. What causes these dissecting aneurysms, if in fact this is the diagnosis? This is a problem with which perhaps Dr. Whyte can help us. It is usually a medial necrosis, and not always associated with hypertension as far as I know, although I believe diabetics are more liable than the rest of the population. The murmur is interesting from the clinician's point of view, in that it was rough, harsh and systolic in time. One must think of aortic sclerosis, aortic stenosis—although the blood pressure was against this, aneurysm and hypertension. She certainly had hypertension, and I believe she probably had aortic sclerosis as well. She had some heart enlargement to go with the hypertension. I have no hesitation in saying that this woman had a dissecting aneurysm of the aorta, and that its extent was fairly widespread, at least down to the abdominal aorta.

Dr. H. M. Whyte: I think without doubt that if one saw this rather obese lady giving this story, one would

have to think of coronary occlusion straight off. And then, finding these blood pressure readings dropping progressively, and the temperature going up, and the blood pressure being unequal in the arms, one has to think of dissecting aneurysm and one cannot get past it. So, having made it easy like everyone else, I now propose to make it more difficult.

First of all, she is an obese lady, she is plump and rather florid, she is lying in bed not at all distressed, and yet her blood pressure is falling. Why is it falling? She could be bleeding, of course; but there is no evidence of that. She had diarrhœa—it was not a black stool, I take it? At any rate, she is still florid, even though her blood pressure is halved. It is unlikely she bled to that extent, I suppose. Moreover, I would like to know why she was hypertensive. Her blood pressure was 240/140 mm. of mercury when seen at one stage, and she had apparently had it for three years. Her mother died in childbirth at an early age, so we do not really know if it was hereditary. She has some evidence now of urinary infection, but nothing in the past. There is the question of phæochromocytoma, but that seems unlikely.

DR. LEWIS: I do not remember whether I mentioned the possibility of polycythæmia, which came to mind because she was florid. But there were no associated signs of that.

DR. WHYTE: The other thing we do not know is how long she was hypertensive. Nor do we know whether it was benign or malignant—do we?

DR. LEWIS: I take it to be not malignant, as we are told the urine was clear and the fundi were not mentioned; but it was said there was no other abnormality found.

DR. WHYTE: Yes, and if it were a recent hypertension, then you would be thinking of associating it with some of these other features, I take it. I would like to know what the femoral pulses were like, to check this dissection. I take it these drenching sweats occurred before this illness. I think the possibilities here are blankets, as mentioned, or aspirin coupled with blankets, especially in view of the arthritis. But if it were in any ways connected with the disease, then I suppose you would have to think of fever—true fever—associated with arthritis, and this, with the blood pressure, would suggest polyarteritis nodosa, as mentioned.

Another thing that I would like to know is what the treatment had been over the previous three years. Although some do not believe that ganglion-blocking drugs will hasten dissection, it has been published that treatment with ganglion-blockers leads to an increased incidence of aortic dissection.

Also, of course, the alcohol must be considered, and beriberi has not been mentioned. To give morphine in beriberi is a bad thing. This patient had morphine, and that could reduce her blood pressure. But there is no evidence of beriberi.

DR. D. JEREMY: Unfortunately no further information is available to answer Dr. Whyte's questions. The examination of the fundi was not noted in the case records.

DR. G. E. BAUER: I saw this patient before she came to hospital. The alcohol, I think, was purely therapeutic, and she was not a chronic alcoholic. I was asked to see her as a possible cardiac infarction, and the striking thing was that when she was admitted to hospital some 12 hours later, although still complaining of pain, she was in no apparent distress. I think it is significant that she died in the circumstances described by Dr. Lewis within a very short period—I think it was 24 hours.

DR. ROSE: Dr. Jeremy will now present the results of the post-mortem examination.

Pathological Report.

DR. JEREMY: The significant post-mortem findings were as follows. The patient had been a small woman of 5 ft. 1 in. in height and weighing 105 lb. The fingers were long for a woman of her stature, and the index finger measured 9·8 cm. In each pleural cavity there was about one ounce of clear fluid. The main abnormalities were found in relation to the heart and great vessels.

There was a large hæmopericardium, with fluid blood and blood clot weighing 10 ounces. Two centimetres above the aortic valve in the ascending aorta there was a clear annular tear, circumferential except for a 2 cm. bridge posteriorly. There was a dissection of the aorta extending as far as the bifurcation. The aorta was the site of moderate atheroma with slight ulceration, but this was limited to its distal parts. There was very little atheroma in the ascending aorta, and there was no scarring to be seen.

The dissection extended about 5 cm. along the left common carotid artery and around the orifice, but not into the left subclavian artery. The right renal artery was considerably narrowed by intimal swelling due to dissecting blood for several centimetres from the origin of the vessel. There was partial occlusion of lesser degree due to slight dissection of the left renal artery.

The aortic valve was bicuspid, with no movement of a third cusp. The valve was heavily calcified and rigid, and this may have produced some stenosis. The left ventricle was markedly hypertrophied. Other valves appeared normal. There was no evidence of myocardial infarction, and no dissection of blood along the coronary vessels. The weight of the heart without great vessels was 14 ounces.

The right kidney was very pale. The capsule stripped easily, and the surface was slightly granular. The cut surface appeared normal. The partial occlusion of its renal artery is described above.

The left kidney was similar to the right, but was congested and not pale. Both kidneys were of normal size.

Microscopic examination of the aorta at the site of dissection and elsewhere failed to show any changes of cystic medionecrosis as described by Erdheim, nor were there any obliterative changes in the vasa vasorum; although some of these vessels were lined by prominent endothelial cells, there was no endarteritis. Vascular bundles extended in places into the media. Elastic tissue stains failed to reveal any gross abnormality of the elastic tissue, which, however, did not appear as regular, as dense or as prominent as in the normal aorta.

There was slight fibrous tissue increase in the myocardium, but no evidence of infarction. There was no significant change in the kidneys.

The final diagnosis was dissecting aneurysm of the aorta with hæmopericardium. The aortic valve was bicuspid and heavily calcified. There was left ventricular hypertrophy.

DR. ROSE: Now that we know the diagnosis, would anyone in the few minutes remaining like to add any comments? Would you, Dr. Bauer, knowing this patient, care to add anything?

DR. BAUER: No, not really. I would like to thank Dr. Lewis for his excellent presentation. It seems all very easy; but when you see this patient lying in a collapsed state, you think you are very clever to make a diagnosis of dissecting aneurysm, but when you find everyone else entirely agrees, it seems you are not so clever after all.

DR. LEWIS: Dr. Hurt did mention the distance of the dissection, which is a point I did not go into. It is interesting that the dissection did involve the renal arteries. When the renal arteries are involved, hæmaturia can occur and the patient may die from renal failure. However, the patient may complain of lumbar backache without having actual dissection of the renal arteries, either due to a retroperitoneal hæmatoma or just due to pain from the dissection referred to the back. Interestingly, in this patient, both loins were tender. This may have enabled us to suggest that perhaps the kidneys were involved.

The other interesting point was the diarrhœa. I did not mention it before, but diarrhœa does occur in dissection of the aorta. That is, of course, excluding cases with mesenteric artery thrombosis, who have blood-stained fæces because of actual infarction of the bowel. A case has been reported in which chronic diarrhœa, going on for some months, was the main symptom of the patient. The reason for it was not given.

Diagnosis.

Dissecting aortic aneurysm.

Correspondence.

CANCER, A DISEASE OF THE NERVOUS SYSTEM.

SIR: May I offer the opinion in reply to Dr. Arthur D'Ombrain (MED. J. AUST., September 12, 1959), that the reverse might be the case, in that "The biological jumps to the psychological". Over a period of years I have attempted some research, very crude perhaps by present orthodox standards, but nevertheless gives results, in that

the life process depends largely on the battle of the proteins and their enzymes intimately linked with the molecule of water. Might I add, it may be surprising to note the number of psychosomatic diseases that present a disturbance of protein metabolism. From this it is not a far jump to a more organic state of disease. Further, that many constitutional diseases which today we call by different names, stem from a common root cause. That the incidence of disease depends on the amount of "fodder" available in the community rather than on statistics.

Yours, etc.,

241 Oxford Street,
Bondi Junction,
Sydney,
September, 21, 1959.

KENNETH ADDISON.

AN IMPROVED METHOD OF PROSTATECTOMY.

SIR: Your Journal of July 11, 1959, has just become available to me. In this issue I was most interested in the article by Mr. Bruce Pearson on "An Improved Method of Prostatectomy".

The results of retropubic prostatectomy are so satisfactory that I think Mr. Pearson will have great difficulty in converting many younger surgeons to his use of a transvesical operation, and in this connexion I should like to comment on some of the points he makes.

1. Without wishing to vie with Mr. Pearson, I would say that a retropublic prostatectomy should take less time than the procedure he advocates. It should certainly seldom take more than 30 minutes, and it often happens that it takes less than the 25 minutes which Millin[1] states as the time required for the operation.

2. If the patient is cystoscoped flat, the preliminary cystoscopy of the retropubic procedure involves little extra time or inconvenience.

3. Prevesical bleeding is not a factor of importance and seldom should arise in a retropubic prostatectomy.

4. Blood in the washings after closing a retropubic prostatectomy should not alarm Mr. Pearson, and "a lot of post-operative lavage" is certainly not the answer. Just leave the catheter alone, and maintain an intravenous drip for the first 24 hours post-operatively (to deliver 3 litres in this time) and drainage will come right (Pyrah *et alii*,[2]).

5. In my opinion it is not, as advocated, an easier procedure than a retropubic prostatectomy. In fact, the only difficulty in any form of prostatectomy is whether or not there is a good plane of cleavage for enucleation. It is in just this case of unexpected difficulty that retropubic prostatectomy is particularly valuable, for one gets an excellent view of the bladder neck for excision of the mass or wedge excision of the posterior bladder neck.

Yours, etc.,

J. M. FORRMAN,
Surgeon.
Colonial War Memorial Hospital,
Suva,
Fiji.
September 19, 1959.

THE CASE AGAINST TONSILLECTOMY.

SIR: I read Dr. Braithwaite's letter in favour of "The Case against Tonsillectomy" with little enthusiasm. It runs so true to type!

Why give so much consideration to the risks, to bad selection of cases, and none to the very great benefits which accrue in properly selected cases? To me it appears like a traffic problem, where certain protagonists might build up arguments to abolish transport, when the matter requiring attention is how to get from one place to another safely and quickly.

After 30 years of active ear, nose and throat practice, I regret I find that many patients who would greatly benefit by tonsillectomy are now denied it because of the modern tendency of which I complain in Dr. Braithwaite's letter. I am as sure of this as I am of the necessity of moving from place to place.

I am now about to have my lunch, and to do so I intend to cross the road, but I will look both ways before I do so. In the same way, before my patients are submitted to tonsillectomy, I satisfy myself operation is indicated, that capable anæsthetists will be in attendance, and that the operation will be carried out under satisfactory conditions. But, Sir, please do not misunderstand me. I am not in favour of indiscriminate tonsillectomy or careless treatment. All I am asking is for those who argue this matter to be fair.

Yours, etc.,

223 Macquarie Street,
Sydney.
September 22, 1959.

A. B. K. WATKINS.

THE CHALLENGE AHEAD.

SIR: We should accept Dr. O'Dea's suggestion (September 19) and examine Marxist "science".

Marxism is dialectical materialism, which means that reality is constituted from contradiction in matter, so that chalk is chalk and is not chalk. "Every organized being is every moment the same and not the same." (Engels.[1])

In this fashion, matter gives to itself perfections which it does not possess, and God is not needed. Nazism and Communism have their common foundation here. God is excluded by introducing a dialecting matter which comes from nothing and from nowhere.

Even knowledge comes from matter, and the reason or root whereby some things know is matter. The same matter is also the root or reason of the non-knowing things. The same is the reason of opposites. And the brain is not the instrument, but the maker of the mind.

The elimination of God means that man loses God-given personal rights. No God, no freedom. For the State is now the only giver of freedom. And, if the State can give freedom it can withhold it. But Engels answers that there is a Marxist freedom, for "freedom is the appreciation of necessity", and you are free so long as you obey the mind of a dictator. Man is entirely for the sake of the State.

Marxism teaches that man belongs in the politico-economic order, and the dialectic, the sole reality, works itself out—slave and slave-owner, peasant and feudal lord, proletariat and capitalist—until the ultimate Marxist heaven of classless society is attained. And in this, there will be no conflict, and no dialectic, and therefore, according to Marxist principles, no reality.

On *a priori* grounds, Marxism is absurd. But we should examine its fruits. First its technological achievements, sputniks, luniks and inter-continental missiles. These are its chief glories. But there is much else. They, the Marxists and the Nazis, invented genocide and "purges". The Marxists even murdered millions of their own farmers —not to mention Koreans, Vietnamese, Hungarians and Tibetans. Their stock retort is that if we go back centuries in history we discover small Christian massacres. But they do not add that these were contrary to Christian precepts, whereas the Marxist massacres are precisely on account of Marxism. And there are the one and a half million fugitives from Marxist countries. There would be millions more, but for the immigration laws on the one side, and the iron curtain on the other side of the frontier. Today, as any of the 224,000 refugees in Australia will tell you, the iron curtain is a double fence of electrified barbed wire, enclosing a strip of land which is mined, overlooked by watch towers, lit by searchlights and patrolled by armed guards with dogs. This "technology" is necessary, not to keep the people of the West from rushing in, but to keep the citizens under Marxism from rushing out. In July, 1959, it was reported to the world's Press from Muong Sing in Laos, by the N.C. News Service of Washington, that the Medical Centre set up in Muong Sing by Dr. Thomas Dooley and other American surgeons is now receiving refugees fleeing before the edict of the communist commissar of Menghwa in China's Yunnan province, that all men and women over 60 who are too feeble for the work programme of the commune are to be executed. So the old folk flee as best they may. But why are diplomats, touring Olympic athletes, North Sea fishermen and others so desperately anxious to escape?

[1] "Modern Trends in Urology", 1953.
[2] *Lancet*, 1955, 2:314.

[1] "Socialism. Utopian and Scientific", 1935, New York, page 47.

But we must admit (for every returning delegation tells us) that the streets have been cleared of flies, stray-dogs, cripples and beggars—all overnight.

And so we find under Marxism a good (their technology, or "pie-in-the-sky"), and a greater evil (the subjection of man to a cruel State tyranny). The good is based upon those natural sciences which were founded under Western civilization and which are now common to the West and to Marxist countries. The evil is proper to Marxism.

Yours, etc.,

Macquarie Street, Sydney.
Undated.

V. J. KINSELLA.

PREMEDICATION OF CHILDREN.

SIR: Sometimes we deal ill with small children, says Dr. McDonald (MED. J. AUST., September 19, 1959), before recommending premedication with methyl-pentynol. Rendell, in 1954, found that 15% of children were tearful and resistant and 85% calm and cooperative when so premedicated; 10% vomited during induction and more at other stages of operation.

Butler[1] in correspondence pointed out that "its effects are, not surprisingly, as varied and to some extent as unpredictable as the more familiar ethyl alcohol". Hodges[2] further drew attention to Rendell's[3] finding that methyl-pentynol prolonged the induction, and that many children retained the unpleasant memory of the incident.

Carrying things to excess, as usual, I confess to having passed Ryle's tubes on four successive cases premedicated with this drug; as the minimum volume aspirated was 8 oz., I abandoned the pose of scientific investigator to which nature has so obviously failed to suit me, and also the use of methyl-pentynol as a premedicant.

If I draw attention to the fact that the most consistent action of alcohols is to promote a free flow of acid gastric juice; that 5 c.cm. of aspirated secretion may produce Mendelssohn's syndrome; and that vomiting and subsequent aspiration are the commonest cause of death in anæsthesia (Edwards *et alii*[4]); may I be forgiven for offering a small dose of hemlock to anyone who suggests that the rather dubious benefits of methyl-pentynol premedication outweigh its undoubted hazards—more particularly under conditions where, of necessity, a large proportion of anæsthetics are administered by doctors without specialist training; of necessity in many places, and of choice in others.

Spare the needle, doctor, and spoil the child?

Yours, etc.,

Lister House,
137 Russell Street,
Toowoomba, Queensland.
September 22, 1959.

I. R. McDONALD.

DANGER FOR DIABETICS.

SIR: In the current enthusiasm for trying out tablets by mouth in place of insulin by injection, many sufferers from diabetes are asking: "Doctor, couldn't I have the tablets, in place of the needles? A friend of mine has got diabetes, and her doctor lets her have tablets."

Physicians will recall the enthusiasm when "Synthalin" tablets were put forward about thirty years ago, and the disappointment over their failure to be of use.

It seems that some kinds of aryl-sulphonyluria drugs now being sold in tablet form will help a few diabetics, perhaps 10% of them. But even then, the long-term results and the risks are uncertain. Years ago the use of "Synthalin" was soon found to be dangerous, and now these new compounds may also prove harmful. At least, their use demands much circumspection.

The fact is that there is no real substitute for insulin. For cases of moderate to severe degree it answers all requirements. Fortunately, most of the drug firms are, with commendable caution, pointing out the limitations of the tablet treatment, and emphasizing the need for care.

[1] *Brit. med. J.*, 1955, 1:44 (January 1).
[2] *Brit. med. J.*, 1955, 1:165 (January 15).
[3] *Brit. med. J.*, 1954, 2:1397 (December 11).
[4] *Anæsthesia*, 1956, 11:194 (July).

Only those who have the disease in mild degree are likely to get help from any of the tablets so far available; in such cases the illness often can satisfactorily—and with more wisdom—be controlled by regulation of the diet. Patients who place themselves on tablet treatment without the direction of the doctor take grave risks. Even when treatment by tablets is thought worth trying, a fortnight or so of careful supervision in hospital, with frequent blood-sugar tests, is wise. For most diabetics, whether on insulin or tablets or neither, care with the diet is still the basis in management.

Yours, etc.,

170 North Terrace,
Adelaide.
September 23, 1959.

A. R. SOUTHWOOD.

References.

DUNCAN, G. G. (1959), *Metabolism*, 8:684.
TUNBRIDGE, R. E. (1959), *Practitioner*, 182:110.

OBITUARY: CHARLES NORMAN PAUL.

SIR: I am sure that Norman Paul would not wish to have an erroneous claim for ever attached to his name. We all know of and appreciate his great services to the public, the medical profession and to Sydney Hospital, and it would be completely foreign to his nature. I refer to the obituary by O. A. Diethelm, in the Journal of August 29, 1959, page 300, where one reads:

> In 1913 he returned to Sydney and commenced consultant practice as a dermatologist . . . He was one of the first, if not the very first, to use radium and later X-ray therapy in his practice.

For details of early X-ray therapy and radium therapy, I refer you to a short paper by Adrian Johnston,[1] entitled "A Note on the Early Use of Radiotherapy in Skin Diseases in Australia". In it one reads that: (i) The earliest recorded X-ray therapy carried out in Sydney for skin diseases was by Herschel Harris and W. J. Munro in 1897 (*Australasian Medical Gazette*, 20:60). (ii) The Sydney Hospital records for the first time in 1900 in its annual report that "advantage too has been taken of the therapeutic use of the Roentgen Rays". (iii) Up till January, 1910, 520 cases of rodent ulcer had been treated at Sydney Hospital. (iv) As regards the therapeutic use of radium, its first recorded use in Australia was by Herman Lawrence in 1903 (in Melbourne).

Incidentally, I have Herschel Harris's old radium records, and the first case recorded by him in his own handwriting was that of a Mrs. Lee, who was referred to him by Dr. McMaster, and who had her first radium application on December 20, 1909.

The amount of therapeutic work that had been carried out by Herschel Harris prior to 1913 was very great; he did not confine his radiological practice to diagnosis only. By 1911 you will read that he had treated 65 cases of ringworm of the scalp; and in the "Transactions of the Ninth Session of the Australasian Medical Congress" (1911) he published "Notes on 20,000 Cases Treated by X-rays".

Also you can read of the work done by W. McMurray in 1901, "Treatment of Lupus Erythematosus", and in 1902 his "Roentgen Rays in the Treatment of the Skin" in "Transactions of the Sixth Session of the Australasian Medical Congress".

In justice to the pioneers, I feel that this short correction should be made, lest an erroneous impression be given abroad of the state of radiotherapy in Sydney in the early days by the statement in the Journal quoted earlier in this letter.

Yours, etc.,

70 Newcastle Street,
Rose Bay, N.S.W.
September 18, 1959.

H. R. SEAR.

A MODIFIED TECHNIQUE FOR ELECTROCARDIOGRAPHY.

SIR: Since the direct-writing electrocardiograph came into general use, the attachment of a neutral or "earthing" lead has become a familiar routine. By convention, the neutral electrode is always located on the right leg of the patient.

[1] *Aust. J. Derm.*, 1954, 2:149 (January).

The technique of setting up for the recording is greatly simplified if the neutral lead is taken from a skin area immediately alongside of the right arm electrode. This permits a paired wire to be connected to that limb, and it matters not which is R.A. and which is neutral, provided that the two electrodes are not in direct contact.

From the patient's viewpoint, his right leg is not "tied down" by the modified technique. From the operator's viewpoint, with two of the five efferent wires identified and attached so readily, the remaining three are easily sorted and less liable to tangle.

The simple modification to the wiring is effected with the aid of some plastic electrical sheathing, or may be incorporated during production.

Yours, etc.,

70 Larmer Street, Narrandera, New South Wales.
Denis T. Burke.

Undated.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE INTERCOLONIAL MEDICAL CONGRESS.[1]

[From the *Australasian Medical Gazette*, March, 1896.]

We are pleased to note that the invitation to Queensland (to sponsor the fifth Intercolonial Medical Congress) emanated from a general meeting of the profession in Brisbane, as unity of the profession is essential to the success of a Medical Congress. A good deal has been heard as to the disunion of the profession in Brisbane—a condition which has largely been brought about, we understand, by that most burning question in all Australian communities, viz., hospital management.

However, this should not now exist, for the principles of hospital management, especially in the larger cities, are now generally accepted, and the white light of general professional opinion should clear up all uncertainties.

Further, there are 2 medical societies in Brisbane. Both have done good work, and able men are to be found in the ranks of each. But we must confess to an earnest wish to see these two welded into one harmonious whole. Doubtless both sides have grievances, and there are difficulties in the way, but they are by no means insuperable. The Queensland Medical Society is the older and wealthier, with a good library and quarters of its own. The British Medical Branch has the advantage of the Journal and the ægis of the parent association. Were these two amalgamated both would gain: there would be one strong society, and the success of the forthcoming Congress would be assured. Were an unanimous invitation from the Brisbane Branch issued to the Medical Society of Queensland, we feel sure that the Society would accept the omende, and would agree to sink all private differences and join the ranks of the local Branch of the largest medical corporation in the world.

Possibly, however, rumour has exaggerated the dissension: if so, union should be easier still.

[1] From the original in the Mitchell Library, Sydney.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-end Course in Surgery at Rachel Forster Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in surgery will be held on Saturday and Sunday, October 31 and November 1, 1959, in the Nurses' Lecture Hall at the Rachel Forster Hospital for Women and Children, Redfern, under the supervision of Dr. Margery Scott-Young. The course is open to all members of the medical profession, and limited accommodation is available for women graduates for the Friday and Saturday nights at an inclusive fee of £2 2s. The programme is as follows:

Saturday, October 31: 9.30 a.m., "Pre-Operative Assessment and Post-Operative Management", Dr. Margery Scott-Young; 11 a.m., "Infections of the Hand", Dr. Richard Opie; 2 p.m., "Femoral and Inguinal Herniæ", Dr. Garven Thomas; 3.30 p.m., "Wounds of the Face, Hands and Genitals", Dr. Margery Scott-Young.

Sunday, November 1: 10 a.m., "Common Surgical Conditions in Children", Dr. A. W. Middleton; 11.30 a.m., "Diagnosis and Management of the Lump in the Breast", Dr. Kathleen Cuningham.

The fee for attendance is £3 3s., and written application, requesting accommodation and enclosing remittance, should be made to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney." The closing date for applications is Friday, October 23, 1959, and a minimum number of five enrolments is required.

Post-Graduate Medical Foundation Grants.

Applications for financial assistance from the Post-Graduate Medical Foundation are now invited. The applications must be addressed to the Post-Graduate Committee in Medicine in the University of Sydney and must be made through or by university departments, hospitals or other institutions or organizations.

Applications should be made on the forms provided. It is expected that the applications will fall under one or more of the following three broad headings: research grants to individuals; educational or research grants to institutions; fellowships at home and abroad. Applications which do not fall under these headings should be made separately in writing and should contain all details.

The necessary forms and any further information may be obtained from the Honorary Director, The Post-Graduate Committee in Medicine in the University of Sydney, 131 Macquarie Street, Sydney, to whom the completed application forms must be returned by noon on Friday, December 4, 1959.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

The following extracts from *Hansard* relate to the proceedings of the House of Representatives.

September 1, 1959.

Hospital Benefits.

Mr. Swartz: I address a question to the Minister for Health. Will Commonwealth hospital benefit be paid to cover patients in a hospital wing in an aged persons' home which is conducted by a public committee? Will it be necessary for such a hospital wing to be registered by a State government as a hospital, in order to attract Commonwealth benefit? What are the conditions under which Commonwealth hospital benefit and Commonwealth additional benefit are paid? What was the total amount paid in all States by the Government during the last financial year? Will the Minister also state the amount of capital subsidy which was paid by the Commonwealth to all States for mental hospitals during the last financial year?

Dr. Donald Cameron: If a section of a home for aged persons run by a committee or organization was set aside as a hospital and recognized as such by the government of a State, it would normally attract the Commonwealth hospital benefit. This benefit is paid for every occupied bed in a recognized hospital. That amounts to 8s. a day and it is deducted from the account a patient receives from the hospital if an account is presented. It is paid to the hospital whether a patient receives an account or not. Commonwealth additional hospital benefit is contingent upon the patient who receives it being a member of a benefit organization. The total amount of Commonwealth benefit, both ordinary benefit and additional benefit, paid in the past twelve months was a little under £15,000,000. That is for the whole of Australia. That money was made available by the Commonwealth Government for the

payment of hospital benefits. The total amount of capital subsidy paid in the last financial year for mental hospitals by the Commonwealth Government to the States was about £1,120,000.

September 2, 1959.

Mental Illness.

MR. WHITLAM asked the Minister for Health, upon notice:

1. Did Dr. Stoller report to his predecessor in 1953 that there was a shortage of 10,962 beds in mental hospitals in that year and that 20,000 more beds would be required by 1965?

2. How many beds had been provided under the States Grants (Mental Institutions) Act 1955?

DR. DONALD CAMERON: The answers to the honorable member's questions are as follows:

1. Yes.

2. Up to 30th June, 1959, the Commonwealth had made grants totalling £4,398,038 to the States under the States Grants (Mental Institutions) Act 1955. The number of new beds provided by the States is not known.

Australian College of General Practitioners.

NEW SOUTH WALES FACULTY.

Meetings in October and November, 1959.

ON Sunday, October 25, 1959, the New South Wales Faculty of the Australian College of General Practitioners is holding a Lecture Demonstration at the Cerebral Surgery and Research Unit at Callan Park at 10 a.m. This is by courtesy of Professor W. H. Trethowan and Dr. Harry Bailey, who will conduct members over the new unit and then demonstrate cases of interest to general practitioners.

The second of the regular annual post-graduate week-end courses will be held at the Ritz Hotel, Leura, from November 13 to 15, 1959. This will be the Annual Pfizer Week-end and the Pfizer Lecturer will be Professor P. M. de Burgh of Sydney, who will speak on "The Newer Viruses". The other guest lecturers and their subjects will be as follows: Mr. C. Murray Maxwell, "Recognition and Management of Congenital Orthopædic Defects"; Dr. J. Adrian Paul, "The Role of the Rehabilitation Centre in Modern Medicine".

The week-end will commence at 5.30 p.m. on Friday, November 13, with cocktails, followed after dinner by several films. Lectures will be held on Saturday afternoon and Sunday morning. The annual competition for the golf trophy, the "Breech Hook" donated by Professor Lorimer Dods and Dr. D. A. Warden, will be held on the Saturday morning, and there will be a dinner dance on the Saturday night. As reservations are limited, early application is advisable. The secretary for both courses is Dr. T. M. Clouston, 9 Babbage Road, Roseville.

Notes and News.

Commonwealth Post-Graduate Awards.

The Commonwealth Government is providing each year a number of awards for post-graduate study and research at Australian universities. One hundred awards will be available in 1960. Graduates or students in the final year of a first degree course are eligible to apply. Applicants must be permanently resident in Australia, but this does not exclude Australians temporarily resident abroad. The awards are for post-graduate study in any field approved by the university at which the award is granted. They are tenable for one year and renewable up to a maximum of four years.

Further information and application forms may be obtained from the Registrar of any Australian university or university college. However, before submitting their applications, intending applicants should consult the head of the university department in which they propose to study. The closing date for applications is the last Friday in November.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 5, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	1(1)	3(2)	..	7(2)	..	..	..	11
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	12	..	12
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	1	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	9(2)	10(9)	7(5)	..	1(1)	..	9	..	36
Diphtheria	1	1(1)	..	..	..	..	..	..	2
Dysentery (Bacillary)	..	1(1)	..	..	4	..	1	..	6
Encephalitis	..	1(1)	..	1	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	53(22)	30(19)	16(1)	10(9)	3(1)	..	..	..	112
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2	1(1)	..	..	..	..	..	..	3
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	1	..	..	..	..	..	..	..	1
Rubella	..	10(12)	..	..	4(4)	..	4	..	27
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	2	19(9)	..	10(15)	1(1)	..	..	..	33
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	1	..	1	..	2
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	25(15)	7(4)	12(7)	4(3)	7(4)	4(2)	1	..	60
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The Fourth International Goitre Conference.

The fourth International Goitre Conference, sponsored jointly by the American Goiter Association and the London Thyroid Club, will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, on July 5 to 8, 1960, under the presidency of Sir Charles Harington, F.R.S. Those wishing to attend who register before December 31, 1959, will pay £1 sterling less than those who register after that date; the closing date for registration is June 1, 1960. Funds for a limited number of travel grants are available. Further information and registration forms may be obtained from the Honorary Secretary, Dr. Selwyn Taylor, 3 Roedean Crescent, London, S.W.15.

Victorian Cancer Congress.

A Cancer Congress, sponsored by the Anti-Cancer Council of Victoria, will be held in Melbourne from August 22 to 25, 1960. The subjects selected for detailed discussion include the following: experimental carcinogenesis; leukæmia; cancer of the lung; cancer and precancerous lesions of the skin; sociological aspects of cancer. Several distinguished visitors and leading Australian authorities will contribute to the discussion. A provisional programme will be available shortly. Membership of the Congress is open to medical graduates and to scientific and social workers in the field of cancer.

Inquiries and applications for registration forms should be addressed to the Honorary Secretary, Victorian Cancer Congress, c.o. Anti-Cancer Council of Victoria, 410 Albert Street, East Melbourne, C.2. Telephone: FB 1386.

Notice.

THE CHILDREN'S MEDICAL RESEARCH FOUNDATION OF N.S.W.

THE following is a list of donations to the Children's Medical Research Foundation of N.S.W. Received from members of the medical profession up to September 8, 1959.

Sir Norman and Lady Gregg (further), £150.

Dr. Ewan Murray-Will (further), £73 10s.

Dr. J. Steigrad (further), £50.

Dr. M. S. Henry, £26 5s.

Western Suburbs Medical Association, £25.

Dr. A. Assef, £21.

Dr. Philip and Dr. Noelene Cappe, £15 15s.

Dr. and Mrs. C. T. Allworth, Dr. and Mrs. Macourt (further), Dr. C. A. Rigg, Dr. Joe Biddulph, Dr. J. N. Chesterman, Dr. Munro S. Alexander, £10 10s.

Dr. E. Cranston, £10.

Dr. D. Kerr Grant, £8 17s. 6d.

Dr. I. and Dr. E. McKinnon, £6 7s. 1d.

Dr. and Mrs. J. Brassey, Dr. and Mrs. W. Deligdish, Dr. and Mrs. William J. Hart, Dr. F. E. Munro, Dr. John R. Coyne, Dr. and Mrs. F. Grunseit, Balmain District Hospital Resident Medical Officers, Dr. Bruce Sinclair-Smith, Dr. I. A. Cooper, Dr. and Mrs. David C. Swan, £5 5s.

Dr. N. M. Kater, Dr. E. A. Hearne, £5.

Dr. D. O. Kinchella, Dr. F. J. Kelleher, Dr. J. A. V. Schofield, £2 2s.

Dr. R. G. Thompson, £1 1s.

Total, £518 11s. 7d. Progress total, £8453 14s. 4d.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Muller, Kurt, M.D., 1938 (Univ. Vienna) (registered under the provisions of Section 17 (2A) of the *Medical Practitioners Act*, 1938-1959), c.o. Wagga Wagga Base Hospital, Wagga Wagga.

Young, Gavan Bernard, M.B., B.S., 1957 (Univ. Sydney), 80 Queen Street, Auburn.

Deaths.

THE following death has been announced:

APPLEFORD.—Sydney Theodore Appleford, on September 20, 1959, at Essendon, Victoria.

Diary for the Month.

OCTOBER 13.—*New South Wales Branch, B.M.A.*: Executive and Finance Committee, Organization and Science Committee.

OCTOBER 14.—Western Australian Branch, B.M.A.: Branch Council.

OCTOBER 19.—Victorian Branch, B.M.A.: Finance Subcommittee.

OCTOBER 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.

OCTOBER 21.—Western Australian Branch, B.M.A.: General Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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